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CARBON MONOXIDE—A DOMESTIC HAZARD

WITH ESPECIAL REFERENCE TO THE PROBLEM
IN WEST VIRGINIA

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As a cause of accidental and suicidal death carbon monoxide ranks second to automobile fatalities. It is estimated that there occur annually in the United States about fifty thousand deaths from asphyxiation, at least half of which are due to this gas. In New York City reports show that for every seven automobile deaths there are five carbon monoxide deaths. Unfortunately, there are few reliable statistics available on the incidence of acute carbon monoxide asphyxiation, and there are none whatever regarding the remote effect of the gas. The most valuable data have been collected and published by the Ohio State Board of Health, which has been emphasizing the importance of the subject from the standpoint of public health for a number of years. The records for 1936 showed a progressive increase of the hazard in both the domestic and the industrial life of the community.

Of a total of 518 gassings, there were 288 from defective domestic appliances, with sixty-two fatalities. Of the victims twenty-three were overcome by bathroom heaters with four deaths, twenty-six by hot water heaters with six deaths, and fifty-five by coal or coke stoves and furnaces with five deaths. The worst menace was the gas stove for heating rooms, which was responsible for twenty deaths. Even the beauty shop is not free from hazard, as eight persons were overcome from imperfect heating devices.

Despite the well known fact that carbon monoxide is a powerful death-dealing agent in acute asphyxiation, knowledge is lacking concerning the delayed result or after-effects of acute asphyxiation or the insidious effect of the gas in producing chronic ailments in those exposed intermittently over long periods. Years ago a statement to the effect that if carbon monoxide does not kill it will do no harm became axiomatic. Unfortunately, absurd as this statement seems, apparently no effort has been made to prove or disprove its correctness. In consequence, victims who have survived asphyxiation and become physically incapacitated have failed to get compensation for disability, nor did the family receive any award in case of death.

It is difficult to estimate the incidence of the so-called chronic forms or secondary syndromes of asphyxiation resulting from carbon monoxide. Until further clinical investigations are made and more careful statistics compiled, it can only be a matter of conjecture.

A personal study and analysis of 150 selected patients suffering either from anoxemia due to slow asphyxiation or from the residual effects of severe acute asphyxiation yielded important facts relating to the subject.

Geographically, the cases were distributed as follows: West Virginia ninety-six, Maryland forty-two, Pennsylvania five, Ohio four, Kentucky, New Jersey and Oklahoma one each.

In our series one out of eleven patients admitted from West Virginia for diagnosis was a victim of slow gas asphyxiation, whereas from all other states combined there was approximately only one out of every 150 patients.

There were ninety-one males and fifty-nine females. In West Virginia the distribution of sex was almost equal, forty-nine males and forty-seven females, while in Maryland there were thirty-two males and only ten females. This difference is attributed to the fact that in Maryland less gas is consumed for heating homes, stores, offices and school rooms, where women are largely employed. Besides, in Baltimore there is an ordinance restricting the sale of gas appliances for domestic use to those approved by sanitary engineers.

Of the group ninety-one were victims of natural gas, twenty-eight of manufactured or illuminating gas, and nineteen of automobile exhaust gas. There were six instances of exposure to both automobile and natural gas and two to automobile and illuminating gas. In four instances the source was coke or coal and blast furnaces.

Among the ninety-six patients from West Virginia five were without occupation. Included in a list of occupations were thirty-three housewives and domestic servants, nine merchants and office employees, nine teachers, eight physicians, six students, three restaurateurs, two attorneys and one minister—a total of seventy-six, or approximately 80 per cent, engaged in nonindustrial pursuits. This is in striking contrast to the situation in Maryland, which is more of an industrial community and where comparatively little natural gas is used for domestic purposes. Among the forty-two patients residing in Maryland there were only three housewives, one physician, one teacher, no students, seven merchants and office employees, one restaurateur, one minister and one attorney—a total of fifteen, or approximately 38 per cent, engaged in nonindustrial pursuits. By occupation, iron, tin and steel mill workers, service men in garages, auto repair men, taxicab drivers and tailors comprised 50 per cent of the patients. These studies furthermore revealed that diseases of the central nervous system, cardiovascular system and gastro-

intestinal system are much more common in persons whose occupations expose them to carbon monoxide over considerable periods of time. Thus in the series of 150 patients studied there were thirteen with symptoms of encephalitis, nine with epilepsy, three with multiple sclerosis and two with tetany. Besides, there were four patients in whom brain tumor was suspected and a number exhibiting marked psychotic and psychoneurotic manifestations.

Vienna records show that laborers engaged in occupations in which they are exposed to carbon monoxide suffer two and one-half times as much from gastrointestinal diseases as those not exposed. The Leipzig statistics show that nearly twice as many become ill and that the number of days for sick leave on account of digestive diseases increased 50 per cent. There is ample clinical evidence to indicate a similar increase in diseases of the heart and blood vessels, but no statistical reports have been found in the literature.

From these studies and investigations it is obvious that the situation is more serious than it appears on

it will be necessary to restate briefly its mode of action when inhaled and the pathologic lesions which result in consequence.

Although carbon monoxide is considered chemically non-toxic, yet when inhaled in sufficient amount it produces a characteristic train of symptoms, the severity and chronicity of which depend on the degree of atmospheric concentration, the frequency and duration of exposure, the temperature and humidity of the air, the amount of physical exercise and the general health and susceptibility of the individual.

While concentrations of 0.01 per cent or less do not give rise to any symptoms, a concentration of 0.02 per cent will cause mild symptoms after several hours' exposure. Thus the safety limit for continuous exposure of industrial workers has been established by health authorities at a concentration level of 0.01 per cent.

The effect of carbon monoxide on the health of an individual is due mainly to the replacement of oxygen, which normally combines with the hemoglobin of the blood, by carbon monoxide, for which hemoglobin has a much greater affinity.

When the blood becomes saturated with carbon monoxide to a degree of 25 or 35 per cent the individual suffers from oxygen deprivation and a state of anoxemia exists. Accordingly, the symptoms of carbon monoxide asphyxiation are primarily those of anoxemia and are similar to those occurring in any other state of anoxemia. Symptoms quite different in character may develop later as secondary manifestations caused by organic tissue changes, the result of severe or persistent anoxemia. These frequently appear as sequelae after partial or even complete symptomatic recovery from acute asphyxia, or after repeated exposure to fluctuating amounts of the gas over prolonged periods.

PATHOLOGIC ANATOMY

There is a remarkable unanimity of opinion with respect to the character and distribution of the pathologic lesions produced by carbon monoxide asphyxiation as witnessed at autopsy by many observers, both in patients and in experimental animals.

Briefly stated, these lesions are fundamentally vascular and may affect any organ. The organs sustaining the greatest damage are those endowed with the richest blood supply, notably the brain and the heart. The pathologic changes consist of dilatation of the peripheral vessels, slowing of the blood stream and increased permeability of the vessel walls, with tendency to hemorrhage, perivascular infiltration and edema.

Although hemorrhages occur most frequently in the capillaries and the smaller vessels and are generally minute, petechial in form and well disseminated, they also occur in larger vessels and in rare instances have caused death.

Coronary thrombosis has repeatedly been observed clinically and at autopsy as well as in experimental animals in states of carbon monoxide anoxemia. The associated lesions of infarction and softening lead to cardiac dilatation, congestion, heart failure and death. Dyspnea, palpitation, cough and precordial pain were among the leading cardiorespiratory symptoms.

On the same underlying pathologic basis, cerebral syndromes develop. Predominant among these is a form of hemorrhagic encephalitis which occurred in 8.6 per cent of our cases. Other lesions of the central nervous system were manifested by symptoms of multiple sclerosis, hemiplegia, tetany, epileptiform seizures, syncopal attacks, emotional episodes, visual disturbances

Increased Incidence of Encephalopathies in Victims of Slow Carbon Monoxide Asphyxiation

Hospital *	Admissions	Encephalitis	Epilepsy	Tetany	Multiple Sclerosis	Ratio of Admissions
Union Memorial..	83,685	48	101	4	21	1:1,819 1:828 1:20,021 1:4,167
Mercy.....	41,415	40	100	1	0	1:1,035 1:391 1:41,415 1:4,602
Diagnostic Clinic	8,112	41	55	6	0	1:198 1:148 1:1,352 1:1,352
Carbon monoxide group	150	13	0	2	3	1:12 1:17 1:75 1:50

* Both Union Memorial and Mercy Hospitals admit all classes of patients. In the Diagnostic Clinic the patients admitted are chiefly those with medical conditions, most of which are of a chronic nature.
† Exclusive of carbon monoxide cases.

casual observation. The chronic ailments with their disabilities and deaths resulting from the remote effects of slow gassing must be reckoned with in order properly to evaluate the full significance of the hazard.

Our studies emphasize the fact that the carbon monoxide problem in the state of West Virginia is quite different from that in the state of Maryland. In the former it appears to be largely domestic, in the latter it is obviously more industrial. As a domestic problem, removal of the danger is fraught with greater difficulty. The best results could be obtained by a campaign of education followed by strict enforcement of laws regulating sanitary and environmental hygiene. This will require thorough organization and complete cooperation between the state board of health, the general medical profession and the lay public. The task confronting those dealing with the problem of carbon monoxide as an industrial hazard is less difficult, as laws have already been enacted which can be better enforced through well organized business groups where the health of the employees becomes a major economic factor.

In order fully to appreciate the manner in which the tissues react to carbon monoxide in producing symptoms of the so-called chronic or delayed forms and residual syndromes of acute carbon monoxide anoxemia,

and various forms of neuroses and psychoses, some with marked mental deterioration.

In the digestive tract were noted such symptoms as glossitis, perversion of taste, cardiospasm, pylorospasm, enterospasm, anorexia, nausea, vomiting and epigastric pain; the latter symptoms were often associated with food ease and hunger pain, simulating ulcer. Many patients suffered from spastic constipation.

In the urogenital domain nocturia, dysuria, albuminuria and glycosuria were the most outstanding features. Functional menstrual disorders in the female and impotence in the male were common symptoms.

Owing to the widespread lesions of the secondary forms of carbon monoxide anoxemia, the symptoms are too varied and bizarre to be presented in the form of a definite clinical picture. The fact is that the symptomatology is representative of multiple syndromes and can be correlated with those caused by similar vascular lesions from other sources affecting the different organs or systems. For a more complete discussion of the clinical aspects of the subject, recourse may be had to our previously published articles.

The following cases, some of which have been previously reported, are cited to illustrate certain clinical forms of slow carbon monoxide asphyxiation:

REPORT OF CASES

CASES 1 and 2.—*History*.—Mr. G. P., a meat cutter aged 25 years, and his wife, aged 23 years, of West Virginia, referred by Dr. Sisler for study and diagnosis, complained chiefly of symptoms from which they suffered in common consisting of headache, weakness, vertigo, neuromuscular pains (shoulder, back and extremities), muscular twitchings, cramps in the toes, numbness and tremor in the legs, staggering gait, cough, anorexia and nausea.

They were both overweight and they both had an abnormally low blood pressure and infected tonsils. All laboratory tests were negative except in the case of Mr. P., who had a red cell count of 5,112,000 with a hemoglobin content of 90 per cent.

The morning they arrived at the clinic it was noted that they both had difficulty in walking. Their gait was slow, hesitating and staggering. The following day there was marked improvement, and the fourth day, on leaving the clinic, they walked perfectly normally. According to their own statement, the headache, neuromuscular pains and weakness in the legs had disappeared and they walked 100 per cent better.

Carbon Monoxide History.—Natural gas was used throughout the house for heating and cooking. There were no open fireplaces and there was no attempt at ventilation. On cold nights they slept with the gas burning in their bedroom. They usually woke up in the morning with headache, which passed off when they got into the open air. The odor of gas was frequently noticed. Their 3 year old boy slept in a room with gas burning and windows closed. He was sickly, pale, too weak to play and vomited every two or three days. The year old baby slept in the room with the parents. It was puny, weak, sickly, pale and suffered with vomiting and diarrhea. Five canaries were kept in an adjoining room heated with gas and unventilated. With the onset of cold weather the birds quit singing, refused food, became weak and shaggy and died one after the other.

A year later Dr. Sisler wrote that after the source of carbon monoxide was removed there was no return of symptoms, and that the children were healthy, robust and had splendid appetites.

This family group represents the simple uncomplicated form of carbon monoxide anoxemia in contradistinction to the more chronic forms exhibiting residual symptoms. This is indicated by the prompt subsidence of all symptoms when the inspired air was freed from the gas and by the subsequent history, which showed that the family escaped the more serious and permanent

after-effects characteristic of the chronic forms. The canaries, which succumb to its effects more readily than human beings, died from slow asphyxiation, and as children, and especially young infants, succumb more readily than adults, it is surprising that they survived. Before suitable chemical tests were available for the detection of dangerous amounts of carbon monoxide gas, canaries were sacrificed for the purpose. Who knows how many infants may have been sacrificed innocently?

CASE 3.—Mr. A. C., a restaurateur aged 29 years, from West Virginia, referred by Dr. Sisler, complained of conditions which corresponded very closely to those described by Mr. and Mrs. P. The outstanding symptoms were weakness, headache, vertigo, nausea, vomiting, dysphagia, ataxia, cough, dyspnea, myalgia, muscular twitchings and stiff and painful joints.

The physical examination was negative except for obesity and absence of patellar reflexes. The blood showed 100 per cent hemoglobin, 7,830,000 erythrocytes and 10,200 leukocytes, with a normal differential count.

For three years he had worked on an average of sixteen hours a day cooking over a gas stove in a restaurant, which was also heated by gas stoves. He also burned gas in the home and, during the winter months, slept with the gas burning in his room. At the restaurant he could often detect the odor of gas, to which he attributed his headache, vertigo, nausea and difficulty in swallowing. He was unable to get relief from these symptoms unless he went outdoors into the open air.

The most interesting feature in this case is the polycythemia, which has considerable diagnostic value. Thirty-six per cent of our patients had a red cell count of over 5,000,000. Davis, who studied the blood of 174 men employed at a blast furnace, found 64 per cent with a red cell count over 5,000,000.

Nasmith and Harrison, by subjecting rabbits and guinea pigs to a carbon monoxide blood saturation of 25 per cent, noted after the third day a steady rise of the erythrocytes until a maximum was reached in three or four weeks, after which the count remained constant. The hemoglobin is also increased but not in the same proportion. In our series it exceeded 100 per cent in nineteen cases. With the exception of occasional leukocytosis no significant changes have been observed in the white cells.

Ten per cent of our cases were associated with various grades of anemia, in which the red cell count was below 4,000,000 and the hemoglobin below 78 per cent. Three of the cases presented a typical picture of pernicious anemia, of which the following two are examples:

CASES 4 and 5.—Mr. and Mrs. C. (husband and wife) of West Virginia, both aged 62, were admitted to Mercy Hospital with symptoms characteristic of advanced Addisonian anemia. The onset, duration, clinical course, symptomatology and objective features were singularly identical in the two patients. The husband's blood showed 60 per cent hemoglobin and 1,766,000 red cells, and the wife's showed 64 per cent hemoglobin and 1,936,000 red cells. Both had gastric achylia and complained of sore tongue, profound weakness, paresthesia, headache, vertigo, stupor, palpitation and dyspnea. The wife recovered after several transfusions and with improved heating conditions. Her hemoglobin rose to 80 per cent and the red cell count to 4,064,000. The husband died despite transfusions.

A common etiologic factor was suspected because of the nature of the illnesses, which seemed strikingly similar in every detail in the husband and wife. On careful inquiry it was ascertained that for eighteen years the family burned gas from their own well for cooking and in open unvented stoves for heating. During the winter months gas was burned continuously day and night in the rooms occupied by the patients without

adequate ventilation. The children, who slept on the second floor without gas heat and with wide open windows, remained healthy. Their dog, which was allowed to occupy the same quarters as the patients, where he spent much of his time sleeping in front of an open fire, was taken ill. He ceased to romp and play, refused food, became weak, sluggish and drowsy and dragged his hind legs when he attempted to walk. He died from the effects of gas in December.

It is doubtful whether or not carbon monoxide alone is responsible for the associated simple or aplastic forms of anemia occasionally occurring in the course of slow asphyxiation. It may possibly be due to an admixture of other gases or vapors contained in natural or illuminating gas. In this particular instance the family burned the unrefined "raw" or "wet" gas from an adjacent well. These unrefined gases are known to contain certain products which have a deleterious effect on the red blood cells.

The nature and severity of the delayed or secondary symptoms seem to vary in different localities. For example, in Ritchie County, W. Va., where there are extensive gas fields and much gas is consumed for domestic purposes in its raw state, lesions of the central nervous system and the heart are very common. Workmen engaged in cleaning and repairing gas wells are particularly susceptible to angina pectoris and organic heart disease. This observation suggests an additional causal factor to that of carbon monoxide attributable to the toxic volatile vapors (pentane, hexane, heptane, octane) which are constituents of natural gas. These are known to produce lesions with symptoms similar to those of carbon monoxide anoxemia. They differ, however, in their effect on the blood, in which there is a tendency to anemia instead of polycythemia.

In order to provide a cross section illustrating the various clinical types of disease resulting from prolonged exposure to the gas, all the patients studied from Ritchie County will be included in the following case reports.

Among this group there were two cases each of encephalitis, tetany and epilepsy and one each of emotional episodes and syncopal attacks. One of the cases of encephalitis was associated with tetany and hypopituitarism and one with coronary thrombosis. There were five cases of angina pectoris, one of which was associated with tetany, and two cases of coronary thrombosis, one associated with encephalitis and one with angina pectoris. A case of carbon monoxide anoxemia was complicated by hypothyroidism. A patient with chronic bronchitis was suspected of having tuberculosis.

CASE 6.—Mrs. G. G., aged 25 years, a housewife of Pemberton, W. Va., gave a history of living in gas-heated rooms for the past twenty years. In recent years she also cooked with gas and slept in a room heated with gas. For the past two years she had been very ill, suffering with vertigo, nausea, daily vomiting, epigastric pain and constipation alternating with diarrhea. Since the onset of illness she had been subject to periodic attacks of what she described as "queer" spells. These occurred at irregular intervals and usually lasted for about half an hour. During these attacks she would lie in a semicomatose state, without muscular spasms but with involuntary bowel movements. These attacks were invariably superinduced by exposure to gas and fluctuated in intensity according to the amount of exposure. She was free during the summer months, when she was not exposed.

After a period of rest, change of environment and improved heating conditions in the home, the vomiting and nervous attacks promptly subsided, her general health improved and she gained 35 pounds (16 Kg.).

CASE 7.—H. A. A., a boy aged 18 years, of Cairo, W. Va., complained of nervousness and gave a history of epilepsy. The first epileptic seizure occurred in November 1935. He had six subsequent attacks prior to examination in May 1936. In February 1936 he discontinued school on account of them. They were characterized by sudden onset, with transient loss of consciousness and clonic spasm of the muscles of the extremities during which he would occasionally bite his tongue. After the attack he would be mentally confused for a short period. The patient's house was heated by burning natural gas in radiant heaters, which were invented. Gas was burned almost continuously in the room he occupied eight or nine hours daily. The following characteristic symptoms were attributed to the gas: headache, vertigo, drowsiness, yawning, dyspnea, palpitation, vomiting and muscular twitchings.

Physical examination showed a normally developed individual of asthenic habits with a blood pressure of 138 systolic and 82 diastolic. He exhibited marked vasomotor disturbances as evidenced by local sweating, abnormal flushing, turgescence of veins and dermatographism. The only abnormal neurologic features were absence of the abdominal and cremasteric reflexes on the right side. The blood showed a hemoglobin content of 97 per cent and a red cell count of 5,230,000, with a normal white cell and differential count. All other tests including the Wassermann were negative.

The patient had one seizure shortly after entering the clinic. He was instructed to improve the heating condition in the home, eat a well balanced nutritious diet and lead a regular hygienic outdoor life.

On December 5, eight months later, his father wrote: "H. has not had a nervous attack since he came home from Baltimore last May. He has gained 23 pounds (10 Kg.) in weight and is heavier than he has ever been. He is strong and vigorous and seems to be as well as he ever was. He takes lots of outdoor exercise such as baseball, long walks and tennis. We are taking every precaution to see that his room is well ventilated and that there are no fumes in it."

CASE 8.—V. M., a mill worker aged 22 years, of Mole Hill, W. Va., had been subject to epileptic seizures from the age of 12 years. There was no history of epilepsy in the family. He was exposed to gas, which was used in the home for fuel from his childhood. On account of his illness he was closely confined to his home. His mother, who was also closely confined, was suffering from symptoms of anoxemia. His health was good before the onset of the present illness. Until a year previously all the attacks were mild in character and occurred mostly at night, averaging from one to four in number. Since then he had had occasional major attacks. In these attacks he lost consciousness momentarily but never fell. He suffered from dull headache, vertigo, cardiospasm, cramps in the toes, insomnia and constipation, and he frequently became depressed and was highly emotional.

Results of the physical examination and the laboratory studies were essentially negative.

Numerous cases of epilepsy following slow carbon monoxide asphyxiation have been reported. It is also known that gasoline, a constituent of natural gas, as well as benzene may produce epileptiform convulsions; the fact that eight of the nine epileptic patients in this series reside in West Virginia, where natural gas is the chief source of fuel, suggests these volatile constituents as contributory factors. This applies more especially where wet or unrefined gas is used for heating and cooking, since wet gas contains more than three times the amount of gasoline found in dry gas.

These constituents have a somewhat similar effect to that of carbon monoxide in producing lesions, especially of the brain and central nervous system. This may explain why most of the patients residing in Ritchie County suffer from severe organic disease of the central nervous system as compared with those who came under our observation from Morgantown. In the former locality, analysis by the West Virginia Geological Sur-

vey of gas from the wells in the community showed a very much higher percentage of gasoline fractions than the gas from wells in the vicinity of Morgantown, where in some instances little more than traces were found.

Among the rare complications of carbon monoxide anoxemia is tetany, of which the following two cases are examples:

CASE 9.—Mrs. J. W., aged 51, a housewife from Pennsboro, W. Va., complained of peculiar nervous and cardiac attacks. Her daughter, 21 years old, had suffered from convulsions for the past three years. A year previously the patient began to suffer from vertigo and a staggering gait and for the past six months had had paroxysmal pain about the heart, associated with numbness and dull pain in the left arm. She frequently noticed palpitation and cardiac irregularity besides periodic muscular twitchings and spasmodic contractions of the toes and left thumb.

Gas was used for cooking and heating. She slept with a gas stove burning in her bedroom, but as it was defective and gave off "fumes" she would not allow it to burn continuously. Her greatest difficulty was in walking when she first got up in the morning. Among outstanding symptoms were peculiar attacks during which she felt nervous and exhausted and suffered from headache, vertigo and weakness in the legs. These were accompanied by belching and a feeling of discomfort about the heart. In her own words, she felt dazed and like her heart was being squeezed. After her first attack she became emotional, was unable to sleep and cried night and day. In the more severe attacks she had transient loss of consciousness, with considerable jerking of the muscles. Later the attacks became somewhat milder but increased in frequency to as many as six in a single night. All of them were accompanied by typical tetanic spasm affecting both hands and arms, associated with numbness and pain which lasted from ten to fifteen minutes. She could not recollect having had a single attack except during periods when she was burning gas.

On admission to the clinic, examination showed the patient to be somewhat underweight with a sallow skin and marked dermatographia. There were puffiness about the eyes, drooping of the upper lids and injection of the conjunctivas. Except for an occasional extrasystole the heart was normal, and the blood pressure, pulse and temperature were normal. There was muscular hypertonicity, especially of the abdominal muscles, and considerable tenderness was present over both shins. All reflexes were hyperactive. A striking feature was the prompt cessation of the tetanic spasms and heart attacks as well as the headache, vertigo and ataxia, all of which disappeared within three days. The laboratory reports were negative throughout. By changing her heating system she continued to improve. A year later she wrote that she had not had any attacks, that her weight had increased from 109 to 145 pounds (from 49 to 66 Kg.) and, though she had occasional feeling of numbness in the hands and arms, that there had been no muscular spasms.

CASE 10.—Mrs. G. P., aged 27, a housewife from Pennsboro, W. Va., presented symptoms of chronic encephalitis, chronic tetany and hypopituitarism.

Four years before she began to complain of attacks of transient numbness in the left forearm and hand, lasting not over a minute. They continued at intervals, without changing in character or frequency, for three years, after which they increased in frequency and severity. They occurred usually at night, during which she would have two or three attacks associated with outcries but unaccompanied with pain. Later, in December, when in her sixth month of pregnancy, the nocturnal attacks increased in frequency from six to twelve each night and also in severity, being accompanied by severe pain and tonic contractions of the muscles of the left forearm and hand, forming the typical obstetric hand characteristic of tetany.

For two weeks prior to the delivery of her child she was confined to bed, mentally confused and disoriented and in a state of profound stupor from which she could not be easily aroused. During this period of illness the family noticed that there was gas escaping in the room, which was heated by a gas heater without a connecting flue. Her nurse became ill

from the gas the first night on duty and suffered with nausea, vomiting, headache, vertigo and drowsiness. The patient's mother, who nursed her the next night, was also taken ill with nausea, headache and vertigo. The husband, who took the mother's place, spent less time in the room, but he, too, felt ill and suffered from headache, vertigo and loss of appetite. At the end of the week the heating system was changed, and the patient gradually emerged from the stupor with a return of her tetany attacks. However, during the summer months, from July to October, there was a marked diminution in their frequency.

Examination showed a hypopituitary type of individual, 30 pounds (14 Kg.) over the ideal calculated weight, with characteristic fat distribution, infected tonsils, marked vasomotor disturbances, slightly nodular thyroid, drooping eyelids, mydriasis and normal eyegrounds. There was tenderness over the insertion of the masseter muscles; hypertonicity of the skeletal muscles and hyperactive tendon reflexes were present.

Laboratory studies showed a serum calcium level of 9.1 mg., blood sugar 93 mg. and blood cholesterol 174 mg. per hundred cubic centimeters. The blood count, blood urea and urea nitrogen were normal and the Wassermann reaction was negative. There was gastric hyperacidity with slight six hour retention. The basal metabolic rate was -8 per cent, and the spinal fluid was normal. During the spinal puncture a typical attack of tetany developed.

A neurologic examination was made by Dr. Charles Bagley, who stated as his impression that she was suffering either from neoplasm in the right posterior central area or from encephalitis. The former has been practically excluded by the subsequent course of the disease.

Tetany appears to be a rare complication of carbon monoxide asphyxiation, as comparatively few cases have been reported. Therefore it is a rather remarkable coincidence that the only two cases which occurred in our series are included in this small group from Ritchie County. Tetany and epilepsy occasionally occur together in the same person; epilepsy has occurred as a sequel in encephalitis. Epilepsy when associated with encephalitis is due to brain injury especially involving the cortex. Tetany cannot be accounted for in the same manner; it is probably due to the effect of gas on the endocrine glands, especially the parathyroids.

CASE 11.—Mr. G. D., aged 36, a farmer and cattle dealer from Pike, W. Va., referred by Dr. Jones and Dr. Woodyard, presented a history of coronary thrombosis, heart block and symptoms of encephalitis with parkinsonian syndrome.

The mother died of angina pectoris and the father of paralysis agitans. The family lived in the midst of a newly developed oil and gas field, and at the time of the patient's illness there were twenty-nine wells located within a radius of a mile from his residence. For a time the wells were allowed to "flow open." The gaseous vapor of some of these wells was piped up on a hill away from the road, to which it would drift and make traffic dangerous and at times almost impossible. His house was heated day and night by burning the unrefined wet gas in open unventilated heaters. The heater in his bedroom was defective and an odor of gas was detected, for which the doctor ordered better ventilation. When the patient was taken sick in February 1935 with symptoms suggesting influenza, he was confined to this room. He had a temperature of 103 F. He was stuporous, delirious, gasped for breath, broke out in cold perspiration and was nauseated and vomited. Both his wife and sister, who were in attendance, became ill from the gas and suffered from nervousness, headache and vertigo. The patient was later referred to the hospital, where a diagnosis of coronary thrombosis was made. In June, following extraction of teeth, heart block developed, with a pulse rate of 30 per minute and the typical Adams-Stokes syndrome. This condition slowly subsided but he continued to be nervous, emotional and obsessed with fear.

On admission to the clinic Sept. 25, 1935, he was in a highly emotional state, introspective and afraid to be left alone. He was considerably overweight and exhibited the characteristic

features of the parkinsonian syndrome, including the masklike expression, flushed face, dry, desquamating skin, muscular rigidity and inability to feed himself, sit erect or stand and walk unaided. His speech was slow, hesitating and monotonous. The blood pressure and heart measurements were normal. There were occasional extrasystoles associated with a soft systolic murmur at the base. The abdominal reflexes were absent, the plantar reflexes were normal and the deep tendon reflexes were hyperactive. There was marked motor weakness with tremor of the tongue and both hands. The neurologic diagnosis of chronic encephalitis, probably the result of chronic carbon monoxide anoxemia, was confirmed by Dr. Gillis.

Dr. King, who saw him later in consultation, found his heart normal on physical examination except for extrasystoles, and the electrocardiogram was negative except for the extrasystoles.

The only positive laboratory evidence consisted of an occasional trace of sugar in the urine, a red cell count of 5,620,000, a hemoglobin content of 100 per cent, and leukocytosis with 13,000 cells and a normal differential count. The basal metabolic rate was -8.6 per cent.

CASE 12.—Mrs. Z. B. M., aged 48 years, a school teacher from Mole Hill, W. Va., had been living for the past twenty years in a home heated by burning natural gas in open unvented gas heaters. Besides, she had been exposed in her school room, in which she taught for eleven consecutive terms. This room was heated in a similar manner. In both home and school room, gaseous odors could often be detected. As a result of her exposure she suffered not only from a severe form of carbon monoxide anoxemia but also from hypothyroidism, a condition often associated with chronic anoxemia. As a symptom of the latter, severe intolerance to cold developed. In order to sleep, she burned gas in her bedroom at night and resorted to the use of extra heavy blankets. Our clinic records show that on the night of July 1 she slept under two sets of blankets with a hot water bottle.

Although the patient had suffered for many years from headache and nervous symptoms, her condition became progressively worse after an attack during which she had, among many other symptoms, severe headache, nausea, vomiting and diplopia. Since then she had continued to suffer with terrific headache, severe vertigo, weakness, staggering gait with a tendency to fall, cramps in the muscles in the legs and hands, twitching muscles of the face and paresthesia of the arms and legs. Her friends noticed a striking change in her personality.

There were twelve members of the family, all of whom lived in the same home environment and all of whom suffered during the winter months from severe headaches and many of the other symptoms enumerated. They all, including the patient, felt better in the summer than in the winter.

A group of symptoms were referable to thyroid deficiency. These include drowsiness, sighing, retarded memory, lack of concentration, *tinnitus aurium*, *muscae volitantes*, visual hallucinations of seeing animate objects passing, auditory hallucinations of hearing her name called and bells ring, intolerance to cold, dry skin, brittle nails and snapping joints.

After two weeks in the clinic it was noted that symptoms referable to carbon monoxide anoxemia, namely headache, vertigo, ataxia, muscular cramps and fibrillations and paresthesia, had practically all subsided, while those of hypothyroidism were still persisting although they were greatly ameliorated.

In both anoxemia and hypothyroidism the clinical manifestations are almost entirely subjective. The only objective features in the case just presented were a slight degree of facial asymmetry with a tendency of the mouth to deviate to the left, a faint tremor of the tongue, dry skin and brittle nails, scanty axillary and pubic hair, genital hypoplasia, hyperactive tendon reflexes and absence of abdominal reflexes.

The urologic examination showed a chronic form of cystitis and trigonitis. All laboratory reports were negative except that of the basal metabolism rate, which was -19.2 per cent.

The basal metabolism is uniformly low in carbon monoxide anoxemia. In seventy-five cases in which the test was made there was only one (a case of toxic goiter) in which the rate was above normal. In sixty-five cases it was 0 or below, and in forty-four cases it ranged from -10 to -40. The tremor, facial asymmetry and absence of abdominal reflexes suggest the possibility of a mild chronic form of encephalitis. The latter is a frequent complication of carbon monoxide gassing.

CASE 13.—Mr. L. J., aged 55, suffered during the winter months with a severe intractable bronchial cough and symptoms characteristic of anoxemia. On account of these symptoms and the persistence of the cough, tuberculosis was suspected.

He gave a history of overexposure to gas in his office, heated by open heaters, where he spent many hours during the day. Since gas was suspected as a possible cause, examination was deferred three days. By that time the cough as well as all other symptoms had subsided, and the physical examination was negative for tuberculosis. After reconditioning his heating system he remained free from symptoms.

CASE 14.—Mr. S. M. C., aged 55, manager of a tourist camp in Ellenboro, W. Va., complained of acute paroxysmal pain in the left side of the chest, irregular heart and shortness of breath. His father had heart trouble and a brother suffered from angina pectoris.

Seven years previously he began to suffer with palpitation and rapid pulse. He felt nervous and was heart conscious, but no organic disease of the heart was found on examination. Two years previously his heart symptoms became more pronounced. He noticed some intermission of beats with rapid heart action and a pulse rate occasionally as high as 120 per minute. At the same time he began to complain of pain about the heart on exertion such as going up hill, when typical attacks of angina pectoris developed.

Among other symptoms were headache, weakness, vertigo, blurring of vision, neuromuscular pains, cramps in the toes, paresthesia, impotence, constipation, hemorrhoids and dysuria.

Examination showed the heart slightly enlarged, normal in rhythm and free from murmurs. The blood pressure and pulse rate were normal. The prostate was somewhat enlarged. Results of laboratory studies were negative throughout.

The patient heated his house with natural gas supplied from his own wells, which he burned in the "wet," unrefined state. There were nine open heaters in the house. On cold winter nights he slept in a room with the gas burning. Carbon monoxide tests indicated dangerous amounts of gas in some of the rooms occupied. After he was freed from exposure to gas by installation of a central heating plant, his health improved. On examination a year later he stated that he felt better than he had felt for years and that although he had been physically active he had been entirely free from attacks of angina pectoris. A strenuous two days hunting trip in the mountains failed to bring on an attack.

On his last examination, Oct. 10, 1939, he had no recurrence of angina pectoris, his heart was regular and free from murmurs, the electrocardiogram was normal and his general health was excellent.

CASE 15.—Mr. W. L. B., aged 62, from Pennsboro, W. Va., was admitted to the clinic Oct. 16, 1939, complaining of severe paroxysmal pains in his chest. Since 1911 he had been engaged in repairing and cleaning oil and gas wells. He was subjected to the gas and vapors escaping from these wells daily, year in and year out. Both he and his co-workers frequently suffered from nausea, weakness and tremors while at work. These symptoms were always ameliorated by inhaling fresh air. The patient was also exposed to gases in the home, which was heated by radiant heaters, unvented. The odor of gas could frequently be detected.

In January 1938 he began to suffer with dyspnea on exertion. In June there developed attacks of paroxysmal precordial pain which radiated down both arms. The first attack occurred after overexertion while he was working on a well from which much gas escaped. Subsequently he had averaged one attack

about every two weeks. Amyl nitrite promptly relieved the pain, but morphine sulfate gave only partial relief.

In February 1939, while sleeping in a room heated by a gas stove, he contracted headache, vertigo, nausea, dyspnea, weakness, sweating and paresthesia. Since then he had had slight ataxia with muscular soreness, fibrillations and cramps. He had been constipated for the past year and his stools were spastic in character. The physical examination was generally negative. The heart was regular; the sounds were distant; no murmurs were heard. The blood pressure, pulse and temperature were normal. Results of laboratory studies likewise were negative with the exception of the blood, which showed a hemoglobin of .94 per cent, 6,140,000 red cells and 7,000 white cells with a normal differential count. Electrocardiographic studies showed progressive changes in Q_s , T_s and QRS_s , suggesting occlusion of the right coronary artery with damage to the posterior base of the left ventricle.

CASE 16.—Mr. J. G., aged 45 years, from Greenwood, W. Va., worked for years in Ritchie County as a gas well driller and later in a machine shop where he was also exposed to gas. As a child he was healthy except for occasional attacks of tonsillitis and an attack of rheumatism at the age of 20. Three years later he passed the examination for the army, and he spent a year in active service abroad during the World War. The following year a heart lesion was detected but he continued to work until 1927, when he became disabled. His chief symptoms were dyspnea and palpitation. Recently angina pectoris developed, with an average of about one attack every four or five days. It usually occurred on exertion, especially when he was facing cold winds.

The attacks were more frequent in winter, when he spent much of his time in the house in front of an open gas fire. He could recall having had only three attacks during the summer months.

The chief symptoms referable to carbon monoxide anoxemia were headache, vertigo, weakness, neuromuscular pain, fears and anxieties, paresthesia, fibrillating muscles, cramps in the legs and toes, tremors and yawning. On his arrival at the clinic Jan. 10, 1938, the blood showed a carbon monoxide saturation of 18 per cent.

His house was heated with six open stoves, three radiant heaters and three old-fashioned burners, none properly vented. His wife, who was similarly exposed, suffered the same symptoms except that she was free from angina pectoris. The daughter, who taught school and spent less time in the house, remained well.

Examination of the heart showed some enlargement and the characteristic physical signs of mitral stenosis, although the electrocardiogram did not show anything strikingly abnormal.

Laboratory examinations were generally negative.

CASE 17.—Mr. C. E., aged 47 years, from Greenwood, W. Va., complained of shortness of breath and acute heart attacks.

With the exception of twenty-one months while serving in the army, he was daily exposed to gas over a period of twenty-two years in his occupation of drilling and cleaning oil and gas wells in Ritchie County. He was also exposed from the age of 12 years in his home, which was heated by burning raw gas in open heaters. His wife and son both suffered from the effects of the gas, and his brother, 48 years old, who also burned unrefined gas in the home, died suddenly from a heart attack while at work in the same gas and oil fields.

The patient's health was good until a year previously, when he first noticed heart symptoms such as paroxysmal precordial pain, fluttering sensations about the heart and dyspnea on exertion. He progressively got worse until Jan. 3, 1938, when he was no longer able to work. A week later, when he entered the clinic, the blood showed a carbon monoxide saturation of 25 per cent. On the train en route to the clinic he had several typical attacks of angina pectoris. Three weeks before, while eating supper in front of an open fire, he suddenly became blind and remained so for an hour. The symptoms characteristic of severe anoxemia included headache, vertigo, amnesia, confusion, ataxia, tremors, muscular twitchings, paresthesia, perverted taste, anorexia, intestinal cramps, weakness and impotence.

Nothing was found on physical examination to suggest any serious organic disease. The heart was normal in size, rate and rhythm. There was reduplication of the first sound but no murmurs. The electrocardiogram was normal. Laboratory studies showed gastric hyperacidity and a basal metabolic rate of -14.5 per cent. Otherwise the results were negative.

After a period of rest in a more wholesome atmosphere his health was restored, and by reconditioning his heating appliances in the home and exercising greater caution in preventing any unnecessary exposure to gas in his occupation, he has been able to work regularly without recurrence of symptoms.

COMMENT

As previously stated, the central nervous system and the heart sustain the greatest damage in carbon monoxide anoxemia. In the brain the area of predilection for the characteristic hemorrhagic lesions is in the basal ganglions, in which the corpus striatum is especially involved. The lesions in this area cause the clinical manifestations of encephalitis, of which there were thirteen cases in the series, most of them of the parkinsonian type.

In the heart there is also an area of predilection, confined largely to the left ventricle and the papillary muscle of the mitral valve. These hemorrhagic lesions are frequently found at autopsy in human beings or in experimental animals subjected to carbon monoxide.

It is interesting to note the frequency of symptoms of angina pectoris in this small group of cases from Ritchie County, especially among the men who had been working in the gas fields. The increase in the incidence among these workers leads one to suspect causal factors other than carbon monoxide. As previously stated, some of the constituents of "wet" gas, to which they were exposed, namely gasoline fractions, are poisonous and produce symptoms similar to those of carbon monoxide anoxemia. The fact would explain why the incidence of angina pectoris or other myocardial diseases associated with carbon monoxide asphyxiation occurs in a much smaller percentage of cases in Maryland or in districts where no natural gas is consumed.

There has been a prevailing opinion that unless carbon monoxide produces complete loss of consciousness no permanent injury ensues. The result of our investigation does not support this view, as there were only a few histories of loss of consciousness in the entire series. None of the patients suffering with symptoms of angina pectoris gave such a history. This observation is confirmed by Kroetz, who states that pain of an anginal character with typical radiation may appear if the inhalation of gas does not lead to unconsciousness.

The effects of carbon monoxide on the heart have been fully discussed in one of our previously published articles.¹

There is still some question, especially in the minds of those engaged in laboratory research, as to the actual existence of the late or residual manifestations of carbon monoxide anoxemia, but in the minds of the internists and those engaged in industrial medicine there is less doubt. Two of our cases in which autopsy was recently performed support the view regarding the effect of carbon monoxide on the central nervous and cardiovascular systems:

The first was a case of acute poisoning in a woman 56 years of age who died forty-eight hours after the exposure. The brain showed numerous petechial hemorrhages scattered throughout with leukocytic infiltration, areas of focal necrosis and edema.

1. Beck, H. G., and Suter, G. M.: Role of Carbon Monoxide in the Causation of Myocardial Disease, *J. A. M. A.* 110: 1982-1986 (June 11) 1938.

The heart also showed many areas of hemorrhage with focal necrosis, disruption and fragmentation of the muscle fibers.

In the other case a man aged 43, who for twenty years drove a taxicab, had recently suffered from typical carbon monoxide anoxemia as a result of exhaust gas from a leaking engine. Although he never lost consciousness he became incapacitated for work and finally, after many months, died from the effects of the gas.² The autopsy showed:

1. Generalized arteriosclerosis with marked sclerosis of the coronary and cerebral arteries.
2. Organizing and fresh thrombi of the basilar cerebral arteries.
3. Miliary cerebral infarction demonstrated in both cerebrum and cerebellum.
4. Cerebral edema.
5. Moderate cardiac hypertrophy with marked myocardial fibrosis and acute degeneration.

Only a few weeks before his death he was suspected of malingering.

Such evidence, combined with the characteristic clinical symptoms of carbon monoxide anoxemia coupled with a definite history of exposure to gas extending over a long period with relief from symptoms when not exposed, should afford ample proof that carbon monoxide may have a serious and damaging effect on the health, even without a history of severe acute asphyxiation or loss of consciousness.

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THE PRESENT STATUS OF THROMBOCYTOPENIC PURPURA

WITH SPECIAL REFERENCE TO DIAGNOSIS
AND TREATMENT

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The exhibition of purpura as a clinical sign of disease was first ascribed solely to the effects of pestilential fevers. With the demonstration, however, by Denys¹ in 1887 that the purpura of Werlhof is characterized by a lowered level of circulating blood platelets, the clinical purpuric states were definitely shown to consist of thrombocytopenic and nonthrombocytopenic groups. Further differentiation within the thrombocytopenic group has been accomplished slowly since Denys's observations and has depended largely on cumulative experience with known etiologic states in which both purpura and marked thrombocytopenia have been observed to occur. There has thus arisen the practical and important subclassification of thrombocytopenic purpura into two groups—the idiopathic and the symptomatic. This is justified because the successful management of the former often requires life-saving surgery, whereas the latter should be managed strictly by medical means. The reversal of these therapeutic principles may promote disaster to the patient. The present discussion summarizes the current status of thrombocytopenic purpura of the idiopathic or essential type, with particular reference to diagnosis and treatment.

PATHOGENESIS

1. *The Mechanism of the Bleeding Tendency.*—At present the only recognized hematologic abnormality which always occurs in this disease is a marked reduction in the circulating platelet level. Since the vital function of the blood platelet in the physiologic mechanism of blood clotting is well accepted, it would appear that the pathogenesis of bleeding is easily explained. Such, however, is not the case, for it has been occasionally observed that the platelets following the removal of the spleen in essential thrombocytopenic purpura may not be maintained at significantly higher levels and yet all clinical hemorrhagic manifestations disappear. Such atypical responses suggest a somewhat broader basic mechanism, namely (a) the platelet level in the blood may reflect or coincide, albeit imperfectly, with some other more fundamental disturbance in the tissues of the body on which blood coagulation depends and which is influenced by splenectomy (this view has again been championed recently by Tidy²), or (b) the bleeding tendency in this disease may be due to a combination of factors, of which the deficit in platelets is only one. Although it is always hazardous to speculate, it would seem that the second point of view is more likely to approximate the facts. Until there is a more satisfactory answer to such fundamental questions as to why the circulating blood remains fluid in the vascular system but coagulates promptly otherwise, the difficulties in understanding the exact mechanism of hemorrhage in every patient with purpuric manifestations become apparent. Obviously the precise role that the platelet plays in the pathogenesis of this disease must await the discovery of more facts that relate to the many other phases of the blood-coagulation problem.

Suggestions that the capillary bed may be at fault either because of increased permeability in addition to thrombocytopenia³ or because of the inability of the capillaries to contract adequately⁴ provide attractive possible explanations for the cause of bleeding but in this disease are not supported by convincing experimental data. There is very little doubt that a defective endothelial structure may result in bleeding, but that such defects are present in purpura haemorrhagica have not been demonstrated. Nevertheless, the vulnerability of the capillary vessels must be a very important circumstance in preventing the loss of platelets and other blood elements to the tissues. The fact that some persons will show petechiae with platelet counts of 100,000 or above, while others show no hemorrhage at platelet levels below 10,000, may be explained on this basis. The fact that the majority (not all) of the patients afflicted with this disease have a prolonged "bleeding time" has been cited as evidence of some obscure change in the capillary endothelium, but until all the factors which influence the mechanism of this test are known the significance of this observation must remain largely speculative.

No deficiencies in the soluble substances of the blood that have been found essential for blood coagulation can be demonstrated. The fact that the blood obtained in the active stages of this disease forms a clot that retracts either slowly or not at all is directly traceable to the paucity in platelet content. It is probably true that failure of the clot to retract and squeeze out serum results in a lack of firmness and impairs its value as a mechanical plug. This may be granted as a liability for

2. This case has been reported in detail (Beck, H. G.: *Gastrointestinal Symptoms Simulating Ulcer in Chronic Carbon Monoxide Poisoning*, *Rev. Gastroenterol.* 6: 196-207 [May-June] 1939).

From the Department of Medicine, Ohio State University College of Medicine.

1. Denys, J.: *Cellule* 3: 445, 1887.

2. Tidy, H. L.: *Brit. M. J.* 1: 583 (April 7) 1928.

3. Bedson, J. P.: *J. Path. & Bact.* 25: 94 (Jan.) 1922.

4. MacKay, W.: *Quart. J. Med.* 24: 285 (April) 1931.

effective hemostasis and may be of more importance in determining the bleeding tendency than is usually accorded the phenomenon.

2. *The Mechanism of Thrombocytopenia.*—(a) The Spleen: Kaznelson's designation of this disease as "thrombolytische purpura" descriptively presents what is now most widely held as the probable role played by the spleen in the pathogenesis of this disease. The belief that the spleen is chiefly responsible for the thrombocytopenia is due to two facts: (1) sternal marrow studies have consistently revealed normal numbers of normal appearing megakaryocytes in a normal cellular setting, and (2) splenectomy has been followed usually by the prompt reappearance of large numbers of platelets in the peripheral blood with a disappearance of all bleeding tendencies. Because it is difficult to demonstrate increased sequestration and phagocytosis of the platelets in the spleens removed from these

that lysis of effete platelets is perhaps a normal physiologic function of the spleen. An augmentation of this function at times, until it has assumed pathologic proportions, appears most reasonable. Platelet counts

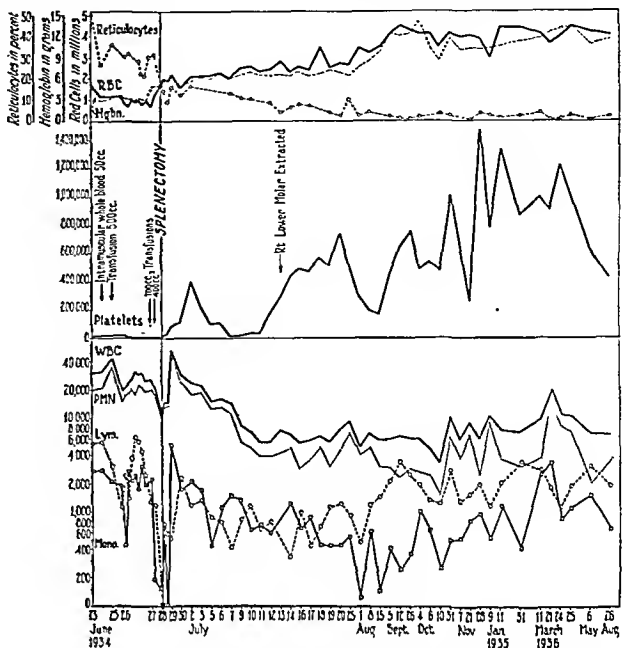


Chart 1 (E. M. R., a girl aged 17 years).—This case illustrates recovery after splenectomy from an acute type of thrombocytopenic purpura. Presenting massive hemorrhage at a platelet level of 3,500 and with red cells of 1,177,000, she was given a transfusion on June 25 without any diminution in the loss of blood. The platelets three days after admission were practically absent from the blood and the red cells had fallen to 800,000. Two transfusions (1,100 cc.) were given on the 27th and operation was decided on. A 110 Gm. spleen was removed the next day. In twenty-four hours the platelets numbered 89,000 with a steady rise to 748,000 by July 25. The secondary temporary dip in platelet level that followed is well shown on this chart and is a very common phenomenon. Charting is on a semilogarithmic scale.

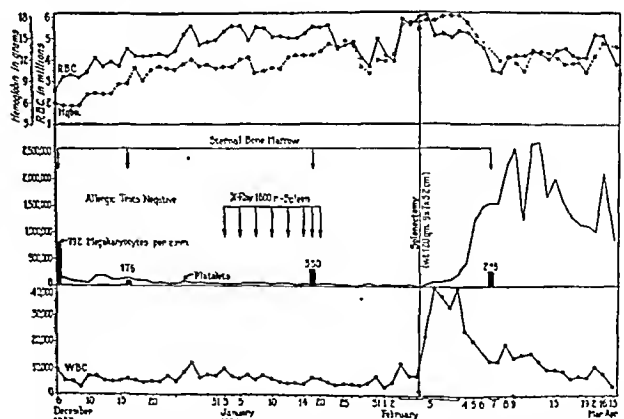


Chart 2 (L. S., a girl aged 14 years).—This case illustrates the actual development of marked depression of the blood platelets from 150,000 to 10,000 per cubic millimeter of blood while the patient was on an elimination diet regimen. After stabilizing at a level of about 10,000 platelets per cubic millimeter of blood for twelve days, she received high voltage roentgen therapy to the spleen on the days shown, each treatment in a dosage of 200 roentgens for a total of 1,600 roentgens. There was no effect on the platelet level or clinical state for the fourteen days following the last treatment. No favorable effect having appeared, splenectomy was accomplished with immediate rise in platelets shown on the chart. Charting is on a semilogarithmic scale.

Comparative Bone Marrow Counts Before and After Splenectomy in Thrombocytopenic Purpura			
Type of Cell	Before Operation* No. per Cu. Mm. "Marrow"	After Operation† No. per Cu. Mm. "Marrow"	
Total Counts			
All nucleated elements.....	211,875	153,837	
Red blood cells.....	3,971,000	3,991,666	
Megakaryocytes.....	152.4	137.8	
W.B.C. : R.B.C. ratio.....	1.7:1	2.2:1	
White Cell Elements			
	Per Cent	Per Cent	
Neutrophilic leukocytes.....	31.9	31.0	
Neutrophilic metamyelocytes.....	3.3	2.7	
Neutrophilic myelocytes O.....	45.6	44.1	
Neutrophilic myelocytes B.....	1.7	3.2	
Neutrophilic myelocytes A.....	0.4	0.7	
Eosinophilic leukocytes (all types)....	4.2	8.3	
Basophilic leukocytes (all types)....	0.6	0.4	
Myeloblasts.....	0.4	0.2	
Small lymphocytes.....	2.5	2.8	
Monocytes.....	0.4	0.7	
Megakaryocytes.....	1.9	1.1	
Red Cell Elements			
	R.B.C. per 200 W.B.C.	R.B.C. per 200 W.B.C.	
	117.6	87.5	
	27.8	33.2	
	13.3	9.0	
Megaloblasts.....	1.6	1.0	
Tissue Cell Elements			
	Per Cent	Per Cent	
	0.1	0.3	
	0.9	4.0	
	0.1	0.7	

This table shows significant increases in levels of megakaryocytes and normoblasts in cases of essential thrombocytopenic purpura preoperatively as compared with the postoperative state. The white cells are not significantly altered, either in number or in type. The change in white blood cell-red blood cell ratio is obviously caused by the postoperative decrease in normoblastic units. It is believed that the increase of erythrogenic tissue before operation is satisfactorily explained on a basis of loss of blood occurring at that time.

* Eleven cases. † Six cases.

patients, owing chiefly to the physical characteristics and the rapidity of lysis of these elements, the exact manner in which the thrombocytopenia is brought about is not regarded as entirely settled. Our own experience with the supravital technic in assaying the specificity of the phagocytic activity of the splenic clasmatoocytes as it relates to the various types of circulating blood elements has convinced us that this mechanism probably accounts for the thrombocytopenia under these circumstances. A possible analogy is seen in the mechanism of the production of anemia in congenital hemolytic icterus and in the recently discovered and described type of severe neutropenia due to excessive granulocyte phagocytosis by splenic clasmatoocytes.⁵ It is believed

5. Wiseman, B. K., and Doan, C. A.: A Newly Recognized Granulopoietic Syndrome Caused by Excessive Splenic Leukolysis and Successfully Treated by Splenectomy, read before the Thirty-First Annual Meeting of the American Society for Clinical Investigation, Atlantic City, N. J., May 1, 1939; abstr., J. Clin. Investigation 18: 473 (July) 1939.

obtained from the splenic artery and vein at operation have yielded inconstant results, but usually the platelet content of the venous blood has been definitely below that of the arterial blood. This has been true in our experience. The accuracy of this procedure in an organ

which sensitively contracts on manipulation, discharging its cellular contents into the vein in unpredictable amount, however, is more than doubtful.

There still remains to be explained the fact that, although the platelets may increase in numbers promptly and symptoms subside with the removal of the spleen, the values for these elements may later fall to the original low levels, with reappearance of the bleeding diathesis. It is usually assumed that either hypertrophy of accessory splenic tissue with clasmatocytic hyperplasia has occurred, or the macrophages of the reticulo-endothelial system in other organs, such as the liver, in taking over the phagocytic function of the spleen also acquire the pathologic overactivity in destroying platelets. This is a reasonable explanation but again lacks adequate supporting evidence. Others have interpreted this fact as invalidating the entire hypothesis of the splenic etiology of the thrombocytopenia in this disease. Frank advanced the theory that the spleen depresses,

are either normal or more often increased in numbers, as shown in the accompanying table. Examination of these cells in the living state in supravital preparations has revealed no qualitative defects in our experience. Cannulization of the efferent vein is probably the only decisive method of determining the functional capacities of these marrow elements, but unfortunately this is not a practical procedure.

A mechanism which may result in peripheral thrombopenia has been suggested by the work of Madison and Squier.⁷ Following their observations on the etiologic relationship between aminopyrine and malignant neutropenia, they noted that when patients with thrombocytopenic purpura were placed on elimination diets the blood platelets returned to normal levels. The fact that the megakaryocyte in some instances does become hypersensitive to specific allergens, particularly to drugs, cannot be doubted (chart 6). These cases should be regarded as symptomatic thrombocytopenic purpura.

In our series of cases, tested by the method of Madison and Squier, there does not appear to be any relationship between the essential type of thrombocytopenic purpura as defined here and the allergic constitution.

PATHOLOGY

Widespread hemorrhage, both gross and microscopic, is the only constant feature found in this disease at necropsy. Most observers have found the bone marrow to be normal, which coincides with our experience. The spleen is usually normal and never more than slightly increased in size. Any case in which the spleen is easily palpated almost surely belongs to the symptomatic group of purpuras. The Nickerson and Sunderland series showed an average weight of 227 Gm. for six spleens removed surgically. The malpighian follicles were found to be enlarged and the germinal centers were active in all but two out of eleven specimens.⁸ Our own studies on the spleens removed surgically have consistently failed to reveal any noteworthy gross abnormalities. The largest spleen in our series of surgical cases weighed 230 Gm., with an average of 124 Gm. We have found nothing noteworthy on study of the paraffin sections. Megakaryocytes are likely to be found in various tissues of the body including the spleen, probably an embolic phenomenon.

INCIDENCE

A study of the literature would indicate that this disease is more common in the female than in the male. In our series of twenty patients, fifteen were females. Approximately three of each five patients had this disease before the age of 21, and more than half before adolescence. It may occur, however, at any age and in any race. The disorder is often congenital, but there is no convincing evidence that it is ever inherited. Not uncommonly ready bruising and other forms of bleeding can be traced through other members of the family tree, but the entire subject of inheritance is beclouded through lack of adequate laboratory data.

HEMATOLOGY

Marked thrombocytopenia is the only constant hematologic feature of the blood. The bleeding time,

7. Squier, T. L., and Madison, F. W.: *J. Allergy* 8: 143 (Jan.) 1937.
8. Nickerson, D. A., and Sunderland, D. A.: *Am. J. Path.* 13: 463 (May) 1937.

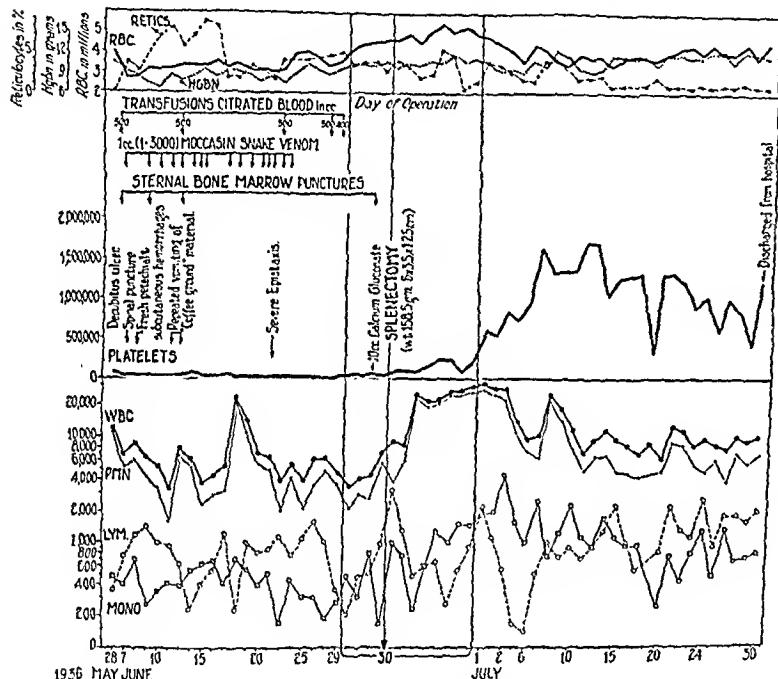


Chart 3 (A. J., a woman aged 61 with idiopathic purpura haemorrhagica).—This chart shows the absence of any rise in platelets after sixteen injections of moccasin snake venom in doses of 1 cc. each. Clinically, there was no diminution in bleeding. After splenectomy the usual rise in platelets immediately followed. The day of operation (June 30) is shown with twelve blood examinations taken at intervals to show the rapidity of rise in platelets after removal of the spleen.

by some as yet unknown method of remote hormone-like control, the megakaryocytes in the bone marrow so that they are functionally unable to supply adequate numbers of platelets. Although this hypothesis cannot be disproved at present, many students of the disease feel that the explanation afforded by the evidence for the theory of splenic cytotoxicity is much sounder. Troland and Lee⁶ have recently reported that extracts of spleens removed from patients with thrombocytopenic purpura contain a substance ("thrombocytopen") which, when injected into the experimental animal, will depress the platelet levels. The attempted duplication of these experiments in our laboratory using monkeys and rabbits has so far failed to substantiate this work.

(b) The Bone Marrow: No evidence has yet been presented which demonstrates any intrinsic pathologic condition of the bone marrow. The megakaryocytes

6. Troland, C. E., and Lee, F. C.: *Bull. Johns Hopkins Hosp.* 62: 85 (Jan.) 1938.

while usually prolonged, has not infrequently been normal in our cases. The clotting time is normal but the clot usually fails to retract. The white cell count may be normal or there may be a mild or moderate increase in polymorphonuclear leukocytes, depending on the severity and recency of hemorrhage. The red cell count and degree of reticulocytosis depend directly on the amount of blood loss. The tourniquet test is usually positive; occasionally, however, it is completely negative even when platelet values are very low.

There is no abnormality in the bone marrow except that which may reflect rapid and excessive loss of blood. The megakaryocytes have never been numerically decreased or qualitatively altered in our cases of true essential thrombocytopenic purpura. Increase in these elements is common. The accompanying table presents the average of twenty-one bone marrow counts in eleven patients preoperatively and the average of fifteen bone marrow counts postoperatively in six patients.

DIFFERENTIAL DIAGNOSIS

The separation of this disease entity from the host of other abnormalities that present bleeding with thrombocytopenia is often a difficult diagnostic problem. Failure to accomplish this maneuver successfully may result in disastrous therapeutic decisions and has, in general, canceled much of the statistical value of the literature. Less attention should be paid to the tourniquet test, clot retraction and bleeding times and more to the diagnostic features given below. The examination of the cellular content of the bone marrow we regard as essential before final diagnosis is made in any given case.

Diagnostic essentials:

1. There must be spontaneous purpura and/or free bleeding from the mucous membranes.
2. The blood platelets must be substantially decreased in numbers, less than 100,000 per cubic millimeter of blood.
3. The clotting time and prothrombin time must be within normal limits.
4. The anemia and leukocyte count must not be out of proportion to the amount of bleeding.
5. There must be no pathologic cells in either the blood or the bone marrow.
6. There must be no recent history of the ingestion of drugs or the occurrence of those diseases known occasionally to produce thrombocytopenia.
7. There must be no appreciable enlargement of the spleen or lymph nodes.

COURSE

In the untreated case, the disease is often characterized by a cyclic course of remissions and exacerbations. Some patients may not have a recurrence of the disease after remission; others may be free for several years only to suffer a relapse later when they regarded themselves permanently cured. In most cases, however, a more or less chronic state ensues with varying degrees of disablement. There does not seem to be any correlation between the severity of the bleeding episode and the subsequent course. In Wintrobe's⁹ series (eighteen cases) the interval between the first bleeding episode and the second varied from one month to twenty-six years.

9. Wintrobe, M. M.; Hanrahan, E. M., Jr., and Thomas, C. B.: *Purpura Haemorrhagica*, with Special Reference to Course and Treatment, *J. A. M. A.* **109**: 1170 (Oct. 19) 1937.

TREATMENT

There have been few diseases in which the status of treatment has been so confused as that of essential thrombocytopenic purpura. This uncertainty has apparently been due in part to errors in differential diagnosis and in part to the failure to appreciate the remarkable tendency of the disease to subside spontaneously.

1. *Medical*.—Radiant Energy: Chief among the forms of radiant energy employed is that of high voltage roentgen therapy over the spleen. This method of treatment, first suggested by Stephan¹⁰ and more recently reviewed by Rudisill¹¹ and others, has been variously reported as successful¹² and unsuccessful.¹³ Our own experience has convinced us that it is worthless (charts 2, 4 and 5). Ultraviolet rays, advocated by Sooy and Moise,¹⁴ have been of no service in our hands nor in those of most others.¹⁵

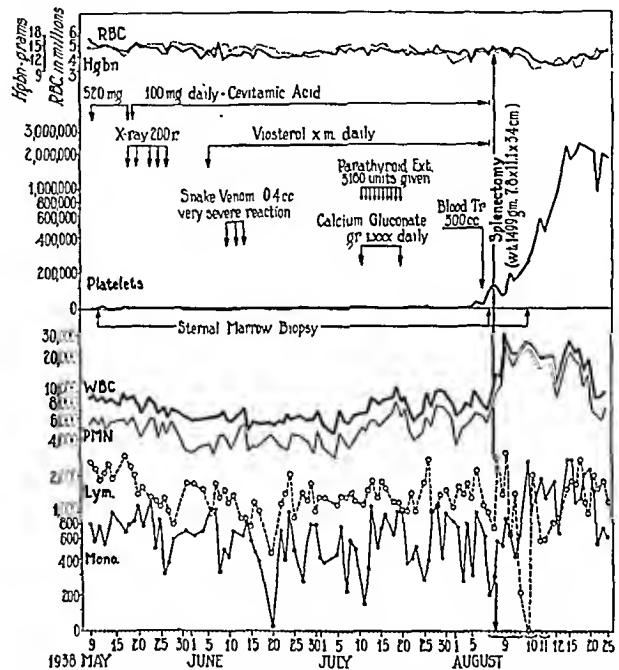


Chart 4 (Z. L., a woman aged 48).—This chart shows, on the same patient, the effects of a number of therapeutic agents variously stated to be of value in thrombocytopenic purpura, and the effects of spontaneous remission and coincident splenectomy. No increased platelet level was observed for ten days after the parathyroid extract treatment had been discontinued. Spontaneous remission then occurred with rising platelet levels. Three days later the platelet level was at 104,000 and splenectomy was accomplished at this level. Under the circumstances of the combined effect of spontaneous remission plus splenectomy, neither the speed in recovery of platelets nor the height to which they soared was greater than in the average case under the effects of splenectomy alone.

Snake Venom: The use of snake venom (Peck and Rosenthal¹⁶) has been suggested both as a means of controlling hemorrhage and as a prognostic test. For treatment from 0.4 cc. to 1 cc. of 1:3,000 moccasin venom is given subcutaneously twice weekly. In Rosen-

10. Stephan, R.: *München. med. Wchnschr.* **67**: 309 (March 12) 1920.
11. Rudisill, H., Jr.: *Successful Treatment of Essential Thrombopenia with Hemorrhage by Roentgen Rays*, *J. A. M. A.* **107**: 2119 (Dec. 26) 1936.
12. Mettier, S. R., and Stone, R. S.: *Am. J. M. Sc.* **191**: 794 (June) 1936.
13. Jones, H. W.; Tocantins, L. M., and Smith, R. M.: *Ann. Int. Med.* **11**: 1311 (April 7) 1938.
14. Sooy, J. W., and Moise, T. S.: *Treatment of Idiopathic Purpura Haemorrhagica by Exposure to Mercury Quartz Lamp: Preliminary Report*, *J. A. M. A.* **87**: 94 (July 10) 1926.
15. Tolstoi, Edward: *Purpura Haemorrhagica (Essential Thrombocytopenia): Treatment by Mercury Vapor Lamp*, *J. A. M. A.* **89**: 370 (July 30) 1927.
16. Peck, S. M.; Rosenthal, Nathan, and Erf, L. A.: *Value of Prognostic Venom Reaction in Thrombocytopenic Purpura*, *J. A. M. A.* **106**: 1783 (May 23) 1936.

thal's series of thirty-four chronic cases twenty-two were improved clinically without any improvement in the platelet levels; the remainder were refractory. The prognostic test is performed by injecting from 0.1 to 0.2 cc. of 1:3,000 moccasin venom intracutaneously. The trend from a positive test to a negative one is said to be of value in estimating the trend of the purpuric state and the prognosis after splenectomy. According to Peck and Rosenthal, patients treated with the snake venom without reversal of the positive skin test to negative are likely to obtain little benefit from surgery. Their experience needs verification from other clinics and further experience before the status of venom therapy is established. In our own hands, with a very limited experience, the use of snake venom has not been encouraging (charts 3 and 4).

Parathyroid Extract: Lowenburg and Ginsburg¹⁷ observed a case of this disease in which the patient received an overdose of parathyroid extract consisting of 500 units in five days. During this time all bleeding stopped. A second case was reported in 1936¹⁸ in which 60 units of parathyroid extract plus calcium

an event which we have not observed. Blood transfusion supplies not only lost plasma volume and red cells but adds also platelets presumably useful in controlling the loss of blood. The practical value of the latter may be open to serious question, but of the former there can scarcely be any doubt. Transfusion has no effect in reestablishing the platelet equilibrium and, therefore, can in no sense be regarded as a curative measure but does serve the purpose of carrying the patient until a spontaneous remission sets in or of preparing the patient for operation so that the surgical risk will be less formidable. In some cases there is a variable hemostatic effect exerted by the transfusions which may be effective for from two to four days. Transfusions, when used, should be given in full doses (500 cc. for those of adult ages) and repeated as often as necessary to: (1) control excessive bleeding, (2) keep the blood pressure above 90 systolic and (3) maintain the red count above 2,000,000. Citrated blood given by the indirect technic is as effective as direct infusions of whole blood. Injections of blood intramuscularly are not of value.

Miscellaneous Measures: The injection of foreign proteins, calcium, proprietary coagulants, epinephrine and the like are without value in this disease. The use of viosterol by mouth has not helped in our cases. Intravenous injections or per oral use of ascorbic acid²⁰ recently advocated has not been of service in other cases²¹ nor in our series (charts 4 and 5). The use of the vitamin substances B₂ and A²² and endocrine extracts, particularly thyrotropic hormone,²³ needs confirmation.

2. Surgical.—Splenectomy: Since the demonstration by Kaznelson and Hess that splenectomy is regularly followed by a return of platelets to the blood stream and the cessation of bleeding, the constancy of this therapeutic result has been amply verified. The dramatic results of removal of the spleen with cessation of hemorrhage, often while the patient is still on the operating table, with a rise of platelets beginning immediately and more often than not reaching normal values in from twenty-four to forty-eight hours, leave one with little doubt that the measure is a specific and not a symptomatic one. The chief problem referable to splenectomy

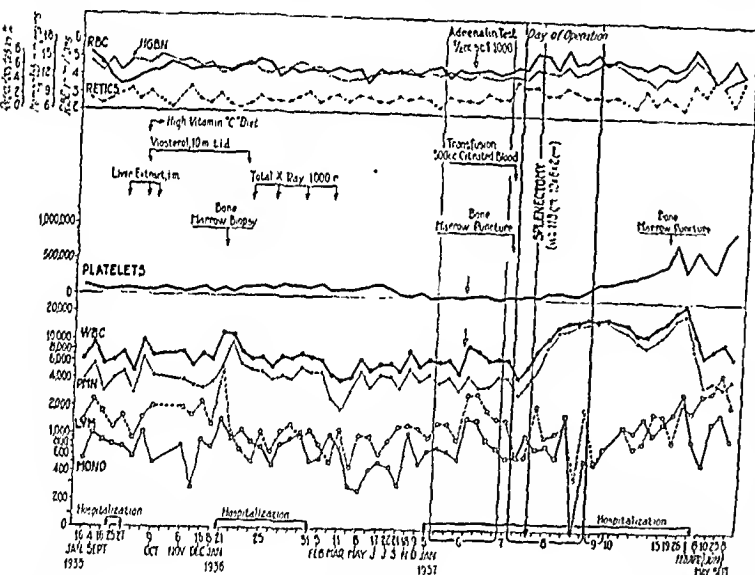


Chart 5 (M. K., a woman aged 50).—This chart illustrates the results of various therapeutic procedures in a very chronic case of thrombocytopenic purpura followed with blood counts over a period of three years, during which time the platelets at no time exceeded 200,000. Splenectomy resulted in a prompt restoration of normal numbers of platelets to the circulating blood.

gluconate were given intentionally to a 7 year old boy with improvement clinically and hematologically. The treatment as outlined by these authors consists in giving parathyroid extract plus calcium gluconate to the point of intoxication in which symptoms of vomiting, progressive weakness, apathy and lethargy predominate. This treatment has been tried in our clinic without any favorable results (chart 4).

Elimination Diets: This is discussed under pathogenesis. The suggestions of Madison and Squier have not been verified in our experience (chart 2).

Transfusion: The value of blood transfusions has been accorded wide acceptance, although Brill and Rosenthal¹⁹ have indicated that an increase of hemorrhage may follow transfusion, especially in acute cases,

becomes a matter of individual judgment as to procedure based on the circumstances surrounding a given individual case. Here, as elsewhere, the wisdom of "treating the patient and not the disease" must not be neglected. The essence of all medical management in this disorder is clearly one of sustaining the patient until a remission occurs. If bleeding does not subside or tend to diminish in the chronic case within a week it would appear unwise to delay surgery further, as it must be accepted as a cardinal principle in the management of this disorder that the more prolonged or violent the bleeding the more danger of a sudden fatal termination through cerebral hemorrhage or bleeding into some other vital structure.

17. Lowenburg, Harry, and Ginsburg, T. M.: Acute Hypercalcemia: Report of Case, J. A. M. A. 99:1166 (Oct. 1) 1932.

18. Lowenburg, Harry, and Ginsburg, T. M.: Induced Hypercalcemia: Its Possible Therapeutic Relation to Thrombocytopenic Purpura, J. A. M. A. 106:1779 (May 23) 1936.

19. Brill, N. E., and Rosenthal, Nathan: Treatment by Splenectomy of Essential Thrombocytopenia, Arch. Int. Med. 32:939 (Dec.) 1923.

20. Miller, D. K., and Rhoads, C. P.: J. Clin. Investigation 15:462 (July) 1936.

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23. Zondek, Hermann, and Kaatz, A.: Brit. M. J. 2:387 (Aug. 22) 1936.

The acute cases especially demand energetic action. Most authors warn against splenectomy in the acute phases of this disease. Our experience, however, has been quite favorable. In our opinion, the incipient acute type as well as the acute exacerbation of the chronic type is an especial indication for urgent surgery, as a goodly proportion of this group will die otherwise. The procedure followed in our clinic may be summarized as follows:

- 1. The diagnosis must be confirmed in all cases by bone marrow examination (puncture technic).
- 2. Blood transfusions are always given immediately if active bleeding presents.
 - (a) If this is effective in stopping hemorrhage after a reasonable trial, delay in advising splenectomy is justified. If the platelet level, determined daily, rises and continues to rise, plans for splenectomy may be temporarily or permanently abandoned, depending on subsequent improvement.
 - (b) If blood loss persists in acute cases in the same or in increased volume, splenectomy is not postponed further.
- 3. Splenectomy is indicated in:
 - (a) Chronic cases if free bleeding persists after a reasonable period of treatment with transfusions or when social or economic factors are important.
 - (b) Acute cases when transfusion is not immediately effective.
- 4. Splenectomy is contraindicated in:
 - (a) Cases of doubtful diagnosis.
 - (b) Cases presenting a recent history of contact with certain drugs.
 - (c) Cases occurring during the active or convalescent stages of all infectious diseases.
 - (d) Cases in which the bone marrow shows depletion of the megakaryocytic content of the bone marrow.

Splenic Artery Ligation: This procedure probably should never be attempted in purpura haemorrhagica. Although the procedure may stop the bleeding,²⁴ this is not to be relied on. The spleens in this disease are small and free from adhesions and are removed with very little more technical difficulty and risk to the patient than the procedure of ligation of the artery.

PROGNOSIS

It is clear that the results in the surgical group of cases vary markedly from clinic to clinic. In our clinic during the past five years there have been nine cases in which splenectomy has been done. One of the patients died of postoperative shock. The others are well at the present time. This is a small series and obviously cannot be used statistically. Surgical deaths will inevitably occur but should not exceed 5 per cent (Giffin's experience²⁵). The liberal use of blood transfusions preoperatively, and postoperatively if required, the adequacy of differential diagnosis and good technical surgery should make it possible to duplicate this low operative mortality in most hospitals.

If not operated on, of those patients in whom bleeding is severe enough to warrant surgery, probably

30 per cent will die (Giffin series 27 per cent). Of those operated on, not more than 3 per cent will have recurrences.

It is not possible to say what the surgical mortality would be in those chronic cases in which expectant or medical treatment is given as they are not usually submitted to surgery. It is obvious that the cases submitted to surgery usually represent the most dangerous risks, which fact tends to weight the surgical mortality to the advantage of the medically treated group. Wintrobe's figures in a series of forty-seven cases at the Johns Hopkins Clinic⁹ in which medical treatment was started after the patient had had the first episode of bleeding showed as late results that 70 per cent continued to have symptoms and signs of varying degree.

SUMMARY

- 1. No single theory for the production of essential thrombocytopenic purpura adequately accounts for all

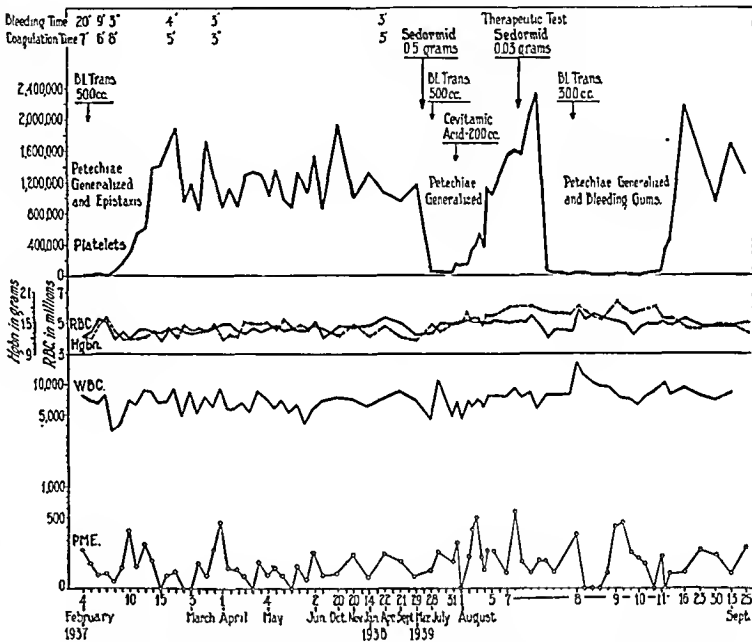


Chart 6 (E. F., a woman aged 57).—This is a case of secondary (symptomatic) thrombocytopenic purpura illustrating the specific platelet-reducing effects of allyl-isopropyl-acetyl-carbamide (sedormid). The patient was admitted to the hospital first in 1937 with the history of ingestion of "barbiturates" and recovery ensued as shown. In July 1939 the patient was again hospitalized with severe thrombocytopenia and hemorrhagic manifestations after having taken 0.5 Gm. of allyl-isopropyl-acetyl-carbamide. After recovery 0.03 Gm. of the drug was given as a test dose. Following a preliminary rise in platelets from 1,600,000 to 2,400,000 per cubic millimeter of blood, these elements fell precipitously to practically zero levels in six hours. Four days elapsed before the platelets reappeared in appreciable numbers. Within twenty-four hours, however, the platelet level was over 800,000 per cubic millimeter of blood.

the known facts relating to this disease; however, that of splenic thrombocytolysis appears to violate the fewest.

- 2. In differential diagnosis, aspiration of bone marrow to rule out leukopenic leukemia, aplastic anemia, pernicious anemia and neoplasia is at times essential. Historical facts relating to drugs and present or recent contact with certain infectious diseases are most important.

- 3. In essential thrombocytopenia, the only measure known that will restore the platelet level is splenectomy. The more pronounced the bleeding tendency the more urgent the indication for surgery.

- 4. No case of symptomatic thrombocytopenia, regardless of the degree of bleeding, should be submitted to surgery.

Kinsman Hall.

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25. Giffin, H. Z.: Internat. Clin. 4: 95 (Dec.) 1936.

TREATMENT OF HYPOPROTHROM-
BINEMIA HAEMORRHAGICA
NEONATORUM(HEMORRHAGIC DISEASE OF THE NEWBORN)
WITH VITAMIN K

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AND

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CHICAGO

More than 250 years has elapsed since the first case of hemorrhagic disease of the newborn was recorded in medical literature and a specific form of treatment was discovered. The events leading up to this discovery form a fascinating chapter in the history of medicine and have recently been reviewed in detail elsewhere.¹ While excellent contributions on the nature of the disease had been made by Lespinasse and Fischer,² Schloss and Commiskey,³ Whipple,⁴ Løvregren,⁵ Rodda,⁶ Gelston⁷ and others, the fundamental observation that served as the impetus for the solution of the exact pathogenesis and treatment of the disease was the investigative work of Henrik Dam, of Denmark.⁸ Dam, in the course of biochemical investigations on sterol metabolism in chicks, found that when they were fed a fat-free diet fatal hemorrhage resulted. Further study showed that the hemorrhagic manifestations were associated with low levels of plasma prothrombin. Because the unknown substance, which was apparently lacking in a fat-free diet, interfered with normal coagulation of the blood, Dam suggested the name vitamin K (K for the Danish word koagulation). Phenomenal progress in the purification and isolation of the antihemorrhagic factor, vitamin K, quickly followed.

Final steps in the application of vitamin K as a prophylactic and curative measure in hemorrhagic disease of the newborn were initiated with the development of satisfactory methods for the quantitative determination of the blood prothrombin level.⁹ Then followed the reemphasis and conclusive demonstration of low prothrombin values in the blood of normal infants as compared with adults¹⁰ and the extreme lowering

of prothrombin levels in infants with hemorrhagic disease of the newborn. Later, a transitory hypoprothrombinemia in normal infants was demonstrated between the second and the sixth day of life.¹¹ This finding explained the earlier observation of Rodda,⁶ who reported prolongation of the clotting time during the same period of life. Finally it was shown that this transitory hypoprothrombinemia and the absolute prothrombin deficiency in infants with hemorrhagic disease of the newborn could be corrected by the administration of vitamin K.

Thus a new era in the treatment of hemorrhagic disease of the newborn may be said to have begun with the work of Waddell, Guerry, Bray and Kelley,¹² who successfully demonstrated the therapeutic effect of vitamin K in two cases of this disease. Their observation was followed by a communication by Waddell and Guerry¹³ on the influence of vitamin K concentrate in shortening the prothrombin clotting time of ten newborn infants as compared with the prothrombin time in untreated babies. These authors¹⁴ further reported eight additional cases of hemorrhagic disease of the newborn, all of which, with the exception of one fatal case, responded to vitamin K therapy with uneventful recovery. A confirmation of these experiences has recently been published by Nygaard¹⁵ and by Dam and his co-workers.¹⁶ From these reports, few as they are, it now appears reasonable to conclude that a fundamental defect in the prothrombin activation of the blood is directly responsible for the bleeding tendencies characteristic of the symptomatology of hemorrhagic disease of the newborn. On etiologic grounds Nygaard proposed the term "hypoprothrombinemia haemorrhagica neonatorum," but more accurately the disease should be designated as "hypoprothrombinemia haemorrhagica neonatorum," since the defect lies in the prothrombin activation of the blood.

The evidences proving the specific effect of vitamin K in controlling the concentration of blood prothrombin in such conditions as obstructive jaundice, diseases of the liver and certain deficiency diseases of chicks and cattle are rapidly multiplying in the literature. Reports on the therapeutic efficacy of this vitamin on hemorrhagic disease of the newborn, however, are still limited in number, so that additional experiences in this particular field must be obtained in order to make its general use more intelligently recommendable both in obstetric and in pediatric practice. The present communication is intended merely to contribute additional data on the treatment of hypoprothrombinemia of the newborn with vitamin K and its substitutes.

A total of twenty-two cases of hemorrhagic disease of the newborn forms the basis of the present report. In all these cases the prothrombin clotting time was

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Drs. A. H. Parmelee and Joseph Greengard of the Cook County Children's Hospital, Dr. F. H. Falls, head of the Department of Obstetrics and Gynecology, Research and Educational Hospitals, and Dr. Fred A. Adair, chairman of the Department of Obstetrics and Gynecology, Chicago Lying-in Hospital, gave the authors permission to use patients in their respective departments for this study.

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15. Nygaard, K. K.: Prophylactic and Curative Effect of Vitamin K in Hemorrhagic Disease of the Newborn (Hypoprothrombinemia haemorrhagica Neonatorum): Preliminary Report, *Acta obst. & gynec. Scandinav.* **19**: 361, 1939.

16. Dam, Henrik; Tage-Hansen, Erik, and Plum, P.: K-vitaminose hos spæde børn som årsag til haemorrhagisk diathese, *Ugesk. f. læger* **101**: 896 (Aug. 3) 1939.

determined by the micromethod of Kato¹⁷ both before and after the institution of vitamin K therapy. In many instances several follow-up determinations were made at daily intervals for a period of three or four days. The results of these observations are summarized in the accompanying tables.

All the cases included in this series exhibited typical clinical symptoms of bleeding, conforming to the usual description of the disease as reviewed recently

TABLE 1.—Symptoms of Hypoprothrombinemia Haemorrhagica Neonatorum in Twenty-Two Cases

Case	Age at Onset, Hours	Symptoms	Prothrombin Time		Vitamin K, Form, Dose, Route *
			Before Treatment, Seconds	24 Hours After Treatment, Seconds	
1	50	Hematemesis	160	27	K ₃ , (F. S.), 10 mg., oral
2	68	Hematemesis, omphalorrhagia	272	32	K ₃ , (F. S.), 10 mg., oral
3	62	Hematemesis, omphalorrhagia	300+	28	K ₃ , (F. S.), 10 mg., oral
4	43	Hematemesis	154	25	K ₃ , (F. S.), 10 mg., oral
5	49	Omphalorrhagia, melena	300+	26	K ₃ , 1 mg., I.M.
6	60	Omphalorrhagia, melena, hematuria, hematemesis	300+	25	K ₃ , 1 mg., I.M.
7	52	Omphalorrhagia	300+	27	K ₃ , 1 mg., I.M.
8	53	Hematemesis, dermal hemorrhage, cerebral symptoms	300+	23	K ₃ , 1 mg., I.M.
9	42	Hematemesis, melena	300+	24	K ₃ , 1 mg., I.M.
10	96	Cerebral symptoms	300+	26	K ₃ , 1 mg., I.M.
11	53	Hematemesis, melena	250	27	K ₃ , 1 mg., I.M.
12	76	Hematemesis, melena	220	26	K ₃ , 1 mg., I.M.
13	63	Hematemesis	246	23	K ₃ , 1 mg., I.M.
14	24	Hematemesis	300+	23	K ₃ , 1 mg., I.M.
15	38	Hematemesis, cerebral symptoms	300+	26	K ₃ , 1 mg., I.M.
16	40	Melena	200	22	K ₃ , 1 mg., I.M.
17	32	Omphalorrhagia, cephalhematoma, hematuria	300+	26	K ₃ , 1 mg., I.M.
18	51	Hematemesis	272	24	K ₃ , 1 mg., I.M.
19	42	Hematemesis, omphalorrhagia	220	25	K ₃ , (W. S.), 2 mg., subcut.
20	72	Hematemesis	110	34	K ₃ , (W. S.), 2 mg., subcut.
21	96	Dermal hemorrhage, melena, omphalorrhagia	300+	24	K ₃ , (W. S.), 2 mg., subcut.
22	72	Hematemesis	300+	20	K ₃ , (W. S.), 2 mg., subcut.

* F. S. = fat soluble; W. S. = water soluble; I.M. = intramuscularly; subcut. = subcutaneously.

by Javert,¹⁸ Clifford,¹⁹ Salomonsen²⁰ and Quick and Grossman.²¹

The frequency of clinical forms of bleeding in the present series was as follows: hematemesis sixteen cases, melena eight cases, omphalorrhagia eight cases, dermal or cutaneous hemorrhage three cases, cerebral symp-

toms three cases and hematuria two cases. In the majority of instances two or three of these symptoms occurred in the same case.

The average time of onset of hemorrhagic manifestations was fifty-four hours after birth, the earliest being twenty-four hours and the latest ninety-six hours. The distribution of the disease as to race and sex was as follows: white thirteen patients, Negro nine patients; male fifteen patients and female seven patients.

The average prothrombin clotting time in ten cases before treatment was 210 seconds, the shortest being 110 seconds and the longest 272 seconds. In twelve cases before the institution of vitamin therapy the prothrombin time was prolonged beyond five minutes.

The average prothrombin time for all cases during the twenty-four hours following treatment was reduced to twenty-six seconds. In most of the cases, shortening of the prothrombin time could be demonstrated within from two to six hours after the administration of the antihemorrhagic vitamin.

TABLE 2.—Prothrombin Time Before and After Treatment

Case	Before Treatment, Seconds	After Treatment with Vitamin K					
		2 Hrs., Seconds	6 Hrs., Seconds	24 Hrs., Seconds	48 Hrs., Seconds	72 Hrs., Seconds	96 Hrs., Seconds
1a	160	80	36	27	26	24	24
2a	272	124	39	32	23	26	27
3a	300+	300+	65	28	27	25	24
4a	154	130	50	25	24	24	22
5b	300+	212	90	26	25	26	24
6b	300+	25
7b	300+	140	65	27	26	23	25
8b	300+	28
9b	300+	166	42	24	24	23	24
10b	300+	170	36	26
11b	250	143	40	27	26	25	24
12b	220	78	34	26	25	24	23
13b	246	29
14b	300+	217	36	23	26	25	26
15b	300+	210	43	26	24	25	23
16b	200	124	33	22	23	22	22
17b	300+	120	...	26
18b	272	63	30	24
19c	220	90	34	25	25	24	24
20c	110	34	30
21c	300+	24
22c	300+	20

a = K₃, (F. S.), oral, 10 mg.; b = K₃, intramuscular, 1 mg.; c = K₃, (W. S.), subcutaneous, 2 mg.

The preparations of vitamin K^{21a} used in our series were (1) 2 methyl-1, 4 naphthoquinone (vitamin K₃), (2) 2 methyl-4 amino naphthol hydrochloride (vitamin K₂) and (3) solution of 2 methyl-1, 4 naphthoquinone in sodium bisulfite. The fat soluble preparation (1) was administered by mouth and the water soluble preparations (2) and (3) were given intramuscularly and subcutaneously. While water soluble preparations can be effectively given intravenously, the most accessible routes of administration were purposely chosen for practical reasons.

Neither intravenous nor intramuscular blood was used, since in none of the cases did any sign of severe posthemorrhagic anemia develop. Subcutaneous injections of fluid were given only in the limited number of cases in which pronounced dehydration was exhibited.

In all cases the clinical improvement was both prompt and permanent, and the therapeutic effects of the several vitamin preparations used were practically identical.

COMMENT

Certain features of hypoprothrombinemia haemorrhagica neonatorum as treated by vitamin K deserve special comment. The most important of these, both

17. Kato, Katsuji: Microprothrombin Test with Capillary Whole Blood: A Modification of Quick's Quantitative Method, *Am. J. Clin. Path.* **10**: 147 (Feb.) 1940.

18. Javert, C. T.: Hemorrhagic Disease of the Newborn, *Am. J. Obst. & Gynec.* **35**: 200 (Feb.) 1938.

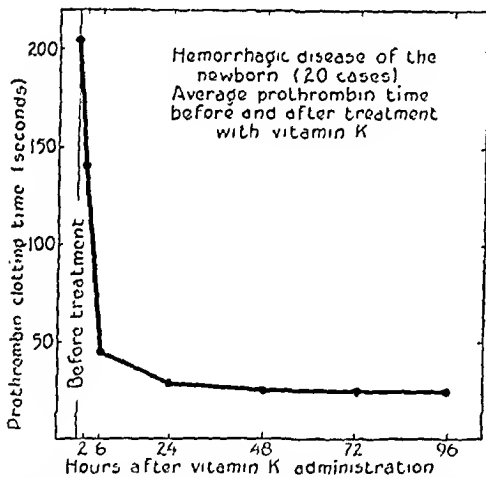
19. Clifford, S. H.: Hemorrhagic Disease of the Newborn: A Critical Consideration, *J. Pediat.* **14**: 333 (March) 1939.

20. Salomonsen, Leif: Morbus Hemorrhagicus Neonatorum (Hypoprothrombinemia Neonatorum), *Acta paediat. (suppl. I)* **27**: 5, 1939.

21. Quick, A. J., and Grossman, A. M.: The Nature of the Hemorrhagic Disease of the Newborn, *Am. J. M. Sc.* **199**: 1 (Jan.) 1940.

21a. Preparations 1, 2 and 3 were supplied by Mead Johnson & Co., Park, Davis & Co. and Abbott Laboratories, respectively.

for diagnosis and for prognosis, are the changes that take place in the prothrombin clotting time of the blood. In a recent study of 173 newborn infants²² it was found that the average prothrombin time on the first day of life, as determined by the micromethod, was 43.2 seconds for the normal mature infants and 46.5 seconds for the premature infants.²³ These values decreased with the growth of the infants, so that by the sixth to the tenth day of life the majority of the infants showed the average normal prothrombin time of approximately twenty-five seconds. In both clinical and subclinical cases of hypoprothrombinemia in the newborn the prothrombin clotting time was markedly prolonged, the average time in ten of our twenty-two cases being 210 seconds. In twelve cases of our series no end point in the microprothrombin tests performed before treatment was recognizable. In other words, when the prothrombin clotting time is prolonged beyond two minutes by the micromethod, even in the absence of clinical symptoms, a presumptive diagnosis of subclinical hypoprothrombinemia must be made. Such an abnormal prolongation of prothrombin time signifies a state of vitamin K deficiency, and replacement therapy is indicated.



Average prothrombin time of twenty of the twenty-two infants before and after treatment with vitamin K.

The specificity of synthetic preparations with vitamin K activity in the restoration of prothrombin activation to its normal level is conclusively proved by our observations, since all cases without exceptions and regardless of the preparations used and the routes of administration responded to the therapeutic action of this vitamin. The efficacy of the treatment with vitamin K appears to be both prompt and permanent. After a single administration of the vitamin, in doses varying from 1 to 10 mg., the prothrombin times dropped within six hours to almost normal levels, as shown in the accompanying chart. The vitamin K preparations used in our series were limited in number, but it is reasonable to expect any chemical substitute embodying vitamin K activity to produce similar effects on the prothrombin time of the blood. The water soluble

analogues of vitamin K used in this study can be injected intravenously with absolute safety, although such a procedure is usually not necessary, since intramuscular or even subcutaneous administration is promptly effective. Various pharmaceutical concerns, now busily engaged in their preparations and assays, expect to offer to the profession a number of water soluble esters of vitamin K. Once the effect of the vitamin has taken place, as evidenced by both cessation of hemorrhage and shortening of the prothrombin time, there is practically no tendency for the clinical signs to reappear. Furthermore, unless the case is complicated by severe posthemorrhagic anemia, the promptness and permanence in the correction of hypoprothrombinemia with vitamin K make blood transfusions unnecessary. In the event of a serious loss of weight or evidence of pronounced dehydration, subcutaneous injections of fluid may be indicated.

Finally it must be emphasized that, in order to treat hypoprothrombinemia in the newborn effectively, an early and correct diagnosis is imperative. In this connection a grouping of hypoprothrombinemia in the newborn into clinical and subclinical types is suggested. The infants who show both the prolongation of blood prothrombin time and actual manifestations of hemorrhage belong to the clinical type of hypoprothrombinemia, while those with only the prolongation of prothrombin time and no clinically demonstrable signs of bleeding constitute the subclinical group. It is indisputable that both forms of hypoprothrombinemia are due to vitamin K deficiency, differing only in degree of such deficiency; hence the specific therapy required is identical in the two groups.

The microprothrombin test recently described by Kato and employed throughout our investigation has been found to be entirely satisfactory and admirably suited for the diagnosis of hypoprothrombinemia in the newborn, since only a small amount of capillary blood is required for the tests, thus facilitating its repetition at frequent intervals on the same patient. The coagulation and bleeding times which customarily serve as diagnostic tests in hemorrhagic diatheses may be prolonged in conditions other than hypoprothrombinemia. It is therefore essential in order to establish the diagnosis of hypoprothrombinemia, whether clinical or subclinical in type, to determine the blood prothrombin time. Moreover, it is safe to expect that frequent or even routine determinations of prothrombin clotting time will result in more frequent detection of subclinical hypoprothrombinemia in the newborn, a condition which may be regarded as a potential or latent form of hemorrhagic disease. It is only with the adoption of such a routine that one can definitely control hemorrhagic tendencies in the neonatal period and thereby reduce the incidence of infant deaths.

SUMMARY AND CONCLUSIONS

Twenty-two infants with hypoprothrombinemia haemorrhagica neonatorum (hemorrhagic disease of the newborn) were successfully treated with synthetic preparations of vitamin K. The infants exhibited the typical clinical manifestations of hematemesis, melena, omphalorrhagia, dermal hemorrhage, hematuria and cerebral symptoms prior to treatment.

In all cases the determinations of prothrombin clotting time by the micromethod were made both before and after the institution of treatment. The average

22. Kato, Katsuji, and Poncher, H. G.: The Prothrombin in the Blood of Newborn Mature and Immature Infants as Determined by the Microprothrombin Test, J. A. M. A. 114:749 (March 2) 1940.

23. These figures represent average determinations done on infants from birth to 24 hours. It was impossible to get the values at birth or immediately thereafter consistently because neither of the authors was resident in the hospital. Consequently, the usual lowering of prothrombin time noted in many infants during the first twelve hours after birth, as reported by other investigators, was obscured.

prothrombin time of ten patients giving a definite end point before treatment was 210 seconds, while in twelve cases the time was prolonged beyond five minutes.

Three synthetic preparations of vitamin K were employed: (1) 2 methyl-1,4 naphthoquinone (vitamin K₃), (2) 2 methyl-4 amino naphthol hydrochloride (vitamin K₅) and aqueous solution of 2 methyl-1,4 naphthoquinone with sodium bisulfite. These drugs were administered orally, intramuscularly and subcutaneously, in the order named, immediately on a definite diagnosis of hemorrhagic disease of the newborn being confirmed by a prolonged prothrombin time. In most of these cases the effect of therapy was demonstrated by the shortening of the prothrombin time within two to six hours after medication. Clinical improvement was both prompt and permanent with all preparations tested.

In none of the cases were blood transfusions given, prompt cessation of bleeding following therapy having caused no alarming loss of blood with consequent anemia. Subcutaneous injections of fluid were employed only in the presence of loss of weight or pronounced dehydration.

From these observations it may be concluded that vitamin K and its esters are specific in the treatment of hypoprothrombinemia haemorrhagica neonatorum.

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LYMPHOSARCOMA

A STUDY OF 196 CASES WITH BIOPSY

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Lymphosarcoma is a malignant neoplastic disease of lymphoid tissue capable of arising in any lymphoid aggregate. It may run an acute or chronic course and is almost invariably very radiosensitive. An apparent cure is possible but the disease is much more likely to terminate in death, at which time the wide extent of clinically unsuspected metastases may be astonishing.

With Hodgkin's disease and lymphatic leukemia, it comprises a group of tumors of relatively low morbidity, the high mortality and often strikingly similar clinical and pathologic pictures of which have properly earned them the designation "malignant lymphomas." (The term "lymphoblastoma" (Desjardins,¹ Minot and Isaacs²) has gained considerable popularity as a means of rather loosely conjoining a number of conditions of which lymphosarcoma and Hodgkin's disease make up the majority.) The practicality and convenience of any term aimed at accomplishing such a linkage cannot be denied when applied to individual cases in which identical clinical settings and often very similar histologic pictures make clearcut differentiation almost impossible, and only as a reminder of these occasional difficulties does the term deserve any merit at all. By implying

a common genesis of the two diseases for which there is actually no justified foundation it has brought about in reported papers a merging of the two conditions in which the distinctive features of each have been lost.

It is our purpose in this paper not to reestablish the separate identities of lymphosarcoma and Hodgkin's disease by any form of detailed differential comparison but rather to present a study of the first named condition by itself, based on a series of 196 cases of lymphosarcoma in each of which the diagnosis was confirmed by biopsy. Moreover, in order to insure uniformity of material no case was included in the group unless diagnosis of the pathologic section had been confirmed at this hospital.

HISTORY

The first recognition of lymphosarcoma as a disease entity to be distinguished from the aleukemic lymphomas (pseudoleukemia) is credited to Kundrat³ (1893). In the succeeding decades various writers attempted to subdivide the aleukemic lymphomas into different distinct types, but the seemingly insurmountable difficulties of drawing sharp lines of demarcation between types and the apparent transition from one type to another have probably led to greater confusion in this branch of oncology than in any other. The concept of lymphosarcoma has not escaped this confusion. From the former simple classification of large and small cell lymphosarcoma, some progress was made in distinguishing between reticulum cell lymphosarcoma^{3a} and malignant lymphocytoma. The giant follicular lymphadenopathy described by Brill, Baehr and Rosenthal⁴ and by Symmers⁵ is usually regarded as bearing some relation to lymphosarcoma, though as yet this relation is not clearly defined, nor has the scope of "Brill-Symmers disease" been adequately determined. The borderlines between lymphosarcoma and lymphatic leukemia, Hodgkin's disease, mycosis fungoides and the reticuloses remain rather shadowy at present. As a reaction to this confusion, the lumping together of thirteen or more different terms into a general category of lymphoblastoma seems an unfortunate defeatist step, hardly serving to make progress in understanding the natural history of what are probably different processes.

MORBID ANATOMY

Just as other tissues may assume malignant properties, so lymphoid tissue is capable of attaining this pathologic mode of expression. The sites of origin of lymphosarcoma are potentially as widespread as is the distribution of lymphoid aggregates throughout the body. The unit of lymphoid tissue, the lymph follicle, being composed of two distinct and easily identified types of cells (the reticulum or endothelioid cells of the germinal center, and the small lymphocytes arranged peripherally about these centers), may give rise to two corresponding histologic types of sarcoma: the reticulum cell type, or reticulum cell lymphosarcoma, illustrated in figure 1, and the lymphocytic type, or malignant lymphocytoma, shown in figure 2 (Ewing⁶). The

From the Memorial Hospital for the Treatment of Cancer and Allied Diseases.

1. Decker, F. H.; Leddy, E. T., and Desjardins, A. U.: Leukopenia and Leukocytes in Lymphoblastoma, *Am. J. Roentgenol.* 39: 747 (May) 1938. Desjardins, A. U.: Radiotherapy for Hodgkin's Disease and Lymphosarcoma, *J. A. M. A.* 99: 1231 (Oct. 8) 1932. Desjardins, A. U., and Ford, Frances A.: Hodgkin's Disease and Lymphosarcoma, *ibid.* 84: 925 (Sept. 15) 1923. Desjardins, A. U., and Watkins, C. H.: Abdominal Lymphoblastoma and Its Treatment by Irradiation, *South. M. J.* 29: 344 (April) 1936.

2. Minot, G. R., and Isaacs, Raphael: Lymphoblastoma and Malignant Lymphoma, *J. A. M. A.* 86: 1185-1189 (April 17), 1265-1270 (April 24) 1926.

3. Kundrat, Hans: Ueber Lymphosarkomatosis, *Wien. klin. Wchnschr.* 6: 211, 1893.

3a. Roulet, F.: Weitere Beiträge zur Kenntnis des Retothelsarkoms der Lymphknoten und anderer Lymphoiden-Organen, *Virchows Arch. f. path. Anat.* 286: 702, 1932.

4. Brill, N. E.; Baehr, George, and Rosenthal, Nathan: Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen, *J. A. M. A.* 84: 668 (Feb. 28) 1925.

5. Symmers, Douglas: Certain Clinical and Pathologic Aspects of Lymphosarcoma, *Am. J. M. Sc.* 174: 9 (July) 1927; Follicular Lymphadenopathy with Splenomegaly, *Arch. Path.* 3: 816 (May) 1927; Giant Follicular Lymphadenopathy With or Without Splenomegaly, *ibid.* 26: 603 (Sept.) 1938.

6. Ewing, James: General Pathology of Lymphosarcoma, *Bull. New York Acad. Med.*, February 1939, p. 92; Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 382.

exact physiologic tie between these two cell types has not been definitely established, although their anatomic juxtaposition bolstered by the clinical observation of the not infrequent termination of reticulum cell lymphosarcoma in lymphatic leukemia strongly suggests the

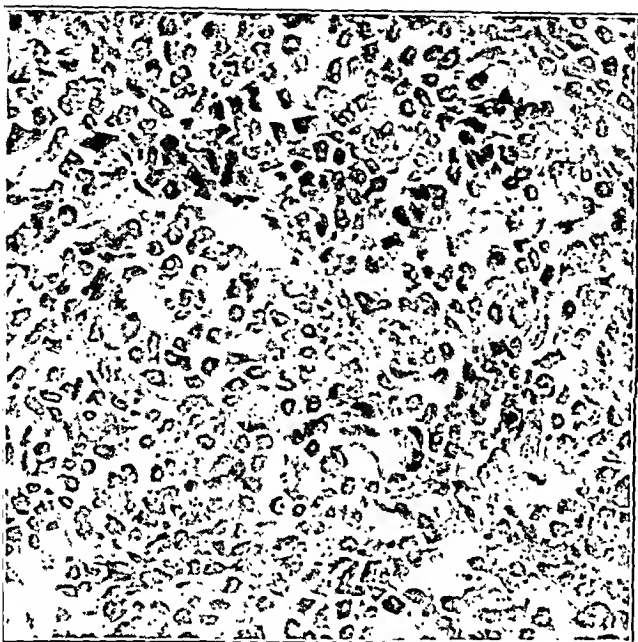


Fig. 1.—Reticulum cell lymphosarcoma ($\times 400$), so-called large cell type; compare size of cells with size of those in figure 2.

existence of a very definite though as yet obscure relationship. It would seem reasonable therefore, until such time as proof to the contrary is found, to consider tumors composed of either cell type, exhibiting malignant properties, simply as variations of the same disease, namely lymphosarcoma.

A predominance either of the cells of the germinal center or of its surrounding lymphocytic zone early in the disease with subsequent obliteration of follicular architecture later results in complete disruption of the structure of the entire lymphoid aggregate. In the case of subepithelial follicle groups there is invasion of the underlying tissues and outward growth of tumor, which may or may not ulcerate. In the lymph nodes there is eventual penetration of the node capsule and invasion of surrounding structures. Though nuclear hyperchromatism may be observed and occasional multinucleated cells are present, it is the general rather than the cytologic picture which provides the essential characteristic. Fibrosis and the presence of a granulomatous element make the diagnosis of lymphosarcoma hazardous.

In 1925 Brill, Baehr and Rosenthal⁴ and in 1927 Symmers⁵ reported several cases of lymphadenopathy often accompanied by splenomegaly, in which the node picture showed "numerical and dimensional follicular hyperplasia" (Symmers). The dimensional increase in the follicle apparently results from proliferation of cells within the germinal center, which enlarges to enormous proportions, often occupying an entire low power microscopic field. This is surrounded by a thinning zone of small lymphocytes, which in many instances has been completely broken through, resulting in a fusion of germinal centers (fig. 3). Whether or not such cases represent a separate clinicopathologic entity is doubtful.

Recently Symmers has stated that in certain instances, at least, a transition to Hodgkin's sarcoma or to a polymorphous cell sarcoma (lymphosarcoma) as evidenced by late biopsies, or to lymphatic leukemia as shown by successive blood counts, may eventually occur in giant follicular lymphoma. The diagnosis of Hodgkin's sarcoma made on tissue removed late in the course of a disease which earlier in its development presented a picture decidedly unlike Hodgkin's granuloma is open to serious question, more so when such tissue also fails to reveal any reactive changes reflecting the earlier influence of the supposed preexistent but now extinct granulomatous process. Such a diagnosis must therefore be based solely on the presence of giant reticulum cells. These, however, occasionally occur in certain forms of lymphosarcoma (giant reticulum cell lymphosarcoma, fig. 4). The late occurrence of a leukemic blood picture is answerable in the same manner, for this is not uncommonly observed in lymphosarcoma. Indeed, the inclination at the Memorial Hospital is to consider giant follicular lymphoma as an early setting for lymphosarcoma, usually destined to run a somewhat less acute but otherwise typical course. Late biopsies in several of our cases have all shown typical reticulum cell lymphosarcoma.

(Exactly where to place Hodgkin's sarcoma (fig. 5) is difficult to decide. Callender⁷ would combine it and reticulum cell lymphosarcoma into a single group called "reticulum cell sarcoma." Hodgkin's sarcoma is undoubtedly a form of reticulum sarcoma developing either late in the course of the more chronic type of Hodgkin's granuloma or earlier in the course of the more acute forms of that disease and representing a truly neoplastic response of the endothelioid cells pre-

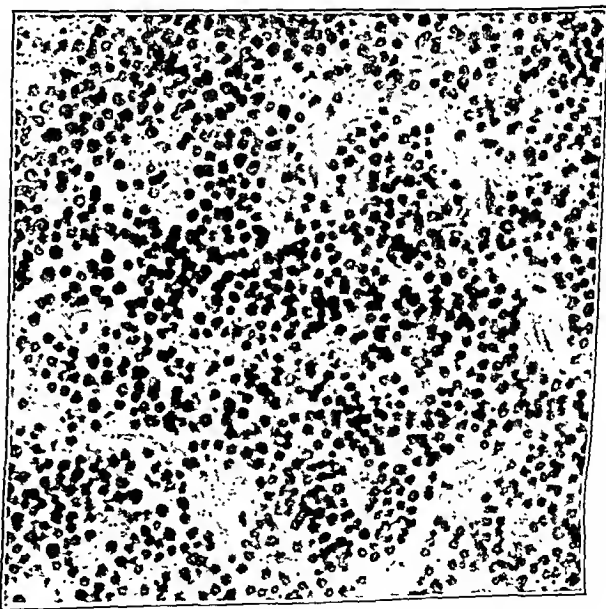


Fig. 2.—Malignant lymphocytoma ($\times 400$), showing diffuse overgrowth of small round cells.

sumably to the exciting agent originally responsible for the chronic inflammatory reaction of the granuloma. These nodes therefore show some reactive fibrosis and perhaps a remnant of the granulomatous element in addition to the reticulum cell overgrowth. Along with

7. Callender, G. R.: Tumors and Tumor-like Conditions of the Lymphocyte, the Myelocyte, the Erythrocyte and the Reticulum Cell, *Am. J. Path.* 10: 443 (July) 1934.

these distinct pathologic differences there are certain clinical variations peculiar to each which still further encourage one to allow them separate identity. For example, reticulum cell lymphosarcoma certainly appears to be a primarily malignant disease whatever its etiology,



Fig. 3.—Giant follicular lymphoma, or Brill-Symmers disease ($\times 50$), demonstrating the marked overgrowth of the follicular germinal centers with thinning and occasional disruption of the surrounding lymphocytic zone.

whereas Hodgkin's sarcoma is presumably superimposed on a granulomatous setting which may completely mask the initiation and progress of the sarcoma. More important, however, is the relationship of the former to the lymphocyte as evidenced by its not infrequent termination in lymphatic leukemia, whereas a leukemic terminus in the latter is not only much less common but is almost invariably of the monocytic type. Therefore Hodgkin's sarcoma has not been included among the cases to be presented here.

ETIOLOGY

Any clearcut statement of the biologic forces inciting lymphoid tissue to malignant growth is as impossible at present as it is for any other type of tissue. As long as histologic appearance and clinical behavior remain the most dependable criteria, it must be assumed that lymphosarcoma is a true neoplasm. Its appearance following the administration of indole^{7a} and estrogens^{7b} and the injection of 1,2,5,6 dibenzanthracene^{7c} indicate that the mechanisms stimulating lymphoid tissue to pathologic new growth are similar to, if not identical with, those activating other tissues.

The frequency with which chronic infections are noted, particularly long-standing inflammatory processes in the upper respiratory system of patients whose first evidence of lymphosarcoma appears as a nodal swelling in the neck, is rather striking. Actually 32 per cent, whose first symptom of lymphosarcoma was cervical adenopathy, complained of some definite chronic infection of the upper respiratory tract. The role of

tuberculosis, however, is much less evident in lymphosarcoma than it is in Hodgkin's disease. It is not inconceivable that prolonged stimulation of lymph nodes may eventuate in malignant cellular activity.

An equally difficult and important question concerns the monocentric versus the multicentric origin of the disease. Lymphosarcoma usually behaves differently from the ordinary forms of carcinoma in several respects. Some of this difference is undoubtedly due to the fact that the former develops within the lymphatic system, this giving it a running start on carcinoma, which must arrive there by process of secondary invasion. Involvement of a chain of lymph nodes by carcinoma is usually progressive, whereas in lymphosarcoma it is often explosive, all the nodes of the entire chain seeming to be simultaneously involved, or the disease may at once involve widely separated node groups, all of which favors the hypothesis that some very readily diffusible activating agent is responsible. On the other hand the observation that early spread of the disease most frequently occurs by means of involvement of contiguous node groups, that tumor nodules are frequently found in organs not ordinarily containing lymphoid aggregates, and that after surgical extirpation of involved nodes patients may remain permanently cured, all strongly suggest that cell emboli alone are responsible. Ewing believes that extension probably involves both dissemination of an exciting agent and cell embolism.)

INCIDENCE

Lymphosarcoma occurs less frequently in this clinic than Hodgkin's disease in the ratio of 3:4. Males are more frequently affected than females in the ratio of

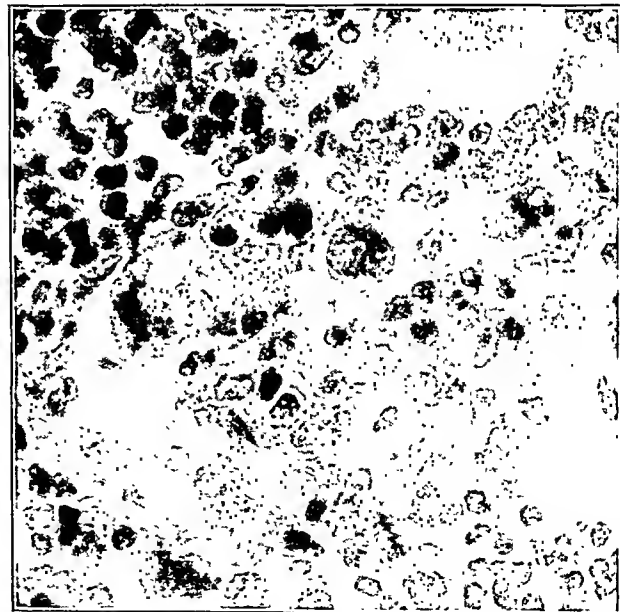


Fig. 4.—Reticulum cell lymphosarcoma with giant cells ($\times 900$). Note the absence of fibrosis. This patient is alive and well six years after cervical dissection and postoperative roentgen therapy.

about 7:3 (1.4:1 in Hodgkin's disease^{7d}). The average age of the two sexes at the time of admission to the hospital was approximately the same, 45 and 45.3 years respectively, about ten years higher than in Hodgkin's disease and somewhat lower than that for the commoner

7a. Büngeler, W.: Die experimentelle Erzeugung von Leukämie, aleukämischen myelosen, Lymphadenosen und Lymphosarkom, *Klin. Wchnschr.* **11**: 1982 (Nov. 26) 1932.

7b. Gardner, W. U.: Estrogens in Carcinogenesis, *Arch. Path.* **27**: 138 (Jan.) 1939.

7c. Lewis, M. R.: Transplantable Lymphosarcoma in Mice, *Am. J. Cancer* **34**: 399 (Nov.) 1938.

7d. Anglem, Thomas: Unpublished Results of a Study of Hodgkin's Disease.

types of cancer, which at this clinic is 53.9 years.⁷⁰ The age distribution in decades is very uniform, not more than 27 per cent of the total number falling within any single decennium (from 50 to 59 years, fig. 5). In general, lymphosarcoma is rare before the age of 20 years and after the age of 70 years. The youngest

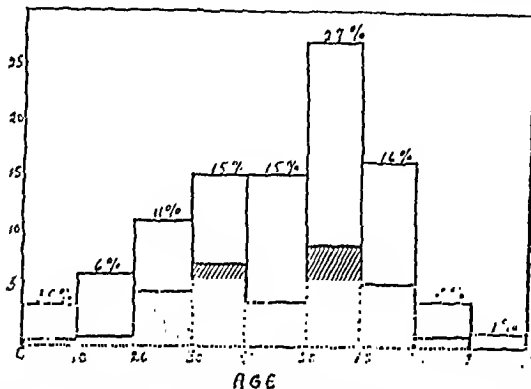


Fig. 5.—The sex and age incidence of lymphosarcoma according to decades, the average age and sex ratio. There were 138 males (white areas) and fifty-nine females (shaded areas), a ratio of 7 to 3. The average age for males was 45 years and for females 45.3 years.

patient was 4 years old and the oldest 88, and one of us has seen a proved case in a woman aged 107.

By far the largest number are of the reticulum cell type (184). Three cases were histologically diagnosed "malignant lymphocytoma" and nine cases presented the microscopic picture of giant follicle lymphoma (Brill-Symmers disease).

In comparison with other types of cancer (such as those of the breast, uterus and oral cavity), lymphosarcoma is not a common disease. The 196 cases here presented represent a collection of twenty years in an active metropolitan tumor clinic, an average of only ten cases a year. It must be reiterated, however, that these constitute only the number in which definitely positive biopsies were obtained but that there exist three other very definite groups: (1) that in which a single biopsy was suggestive but not definite, (2) that in which biopsy was impossible owing to inaccessibility of the disease and (3) that in which the necessary minor surgical procedure was refused by the patient. In each of these groups the subsequent clinical course was characteristic of a malignant lymphoma. Certainly, many of these patients had lymphosarcoma and therefore the figure just given must be taken to represent only an irreducible minimum.

CLINICAL FEATURES

In any disease such as this in which the possible sites of primary growth are not limited to any one organ or tissue but may occur almost anywhere within the body, and in which secondary dissemination eventually becomes widespread, it is obvious that any attempt at enumeration of clinical signs and symptoms would probably become so involved as to be of little practical value. However, it is possible by resorting to generalizations to obtain some information of real diagnostic worth.

Initial Symptom (fig. 6).—Visible and palpable external glandular swelling constituted the first evidence of disease in 65 per cent of the patients. The enlargement was in almost all cases entirely painless, though, in an occasional case in which there was massive swelling in the neck, pain traceable to infiltration of the cervical plexus was present. The amount of nodal

swelling at the time of first examination varied considerably, from that which was hardly visible and barely palpable to masses producing gross physical deformity. Lymphosarcomatous nodes in general tend to have a characteristic resilient firmness not unlike that of uncured gum rubber. Usually the entire chain is involved, but exceptionally a solitary enlarged node may be present. They are more frequently discrete and movable until capsular invasion has taken place, when they tend to become matted together and fixed.

Symptoms referable to the abdomen occurred in 17.5 per cent of cases, and in two thirds of these the main complaint was pain of varying degree, usually little more than a vague discomfort but occasionally sharp and colicky, presumably due to interference with bowel function. Partial or complete intestinal obstruction, indefinite gastric complaints, melena, ascites and a dragging sensation in the abdomen make up the remainder. In 11.6 per cent difficulties of the upper respiratory tract were first complained of (such as sore throat, tonsillar swelling, nasal obstruction and bleeding). Thoracic symptoms were first to appear in only 3.6 per cent (pain, dyspnea, cough, upper mediastinal syndrome). Bone pain occurred initially in 1.83 per cent. Systemic symptoms (chill, fever, lassitude, increased sweating, weight loss) are conspicuously absent in early lymphosarcoma, rarely appearing until the disease has become far advanced.

The general mildness of the symptoms early in the disease is evidenced by the fact that the average duration of time from onset of symptoms to application for advice was 8.7 months.

Primary Site.—It has become traditional in many circles to consider lymphadenopathy in lymphosarcoma as a priori evidence of a primary site of disease in some other tissue or organ drained by the nodes involved. The usual sequence of events in carcinoma has probably given rise to this mental attitude.

In certain instances of rapidly disseminating disease it is impossible to determine whether a given organic

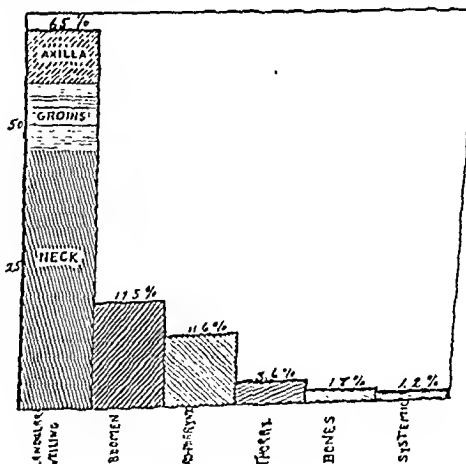


Fig. 6.—Anatomic distribution of the first sign or symptom indicative of disease.

involvement is primary or secondary. Exclusive of such cases, however, an extranodal focus of disease could be found and could reasonably be assumed to represent the primary site in only one third of the patients examined. (In 65 per cent of these (table 1) the primary disease arose in one of the cranial structures with the tonsils and nasopharynx making up the majority. In 16 per cent it arose in the gastrointestinal tract

⁷⁰ Pack, G. T., and LeFevre, R. G.: The Age and Sex Distribution and Incidence of Neoplastic Diseases at the Memorial Hospital, City of New York, *J. Cancer Research* 14: 167 (June) 1930.

(stomach six cases, jejunum two cases, ileum two cases, rectum one case). It is noteworthy that more than half of the gastrointestinal group arose in the stomach. Phillips and Kilgore⁸ found, moreover, that thirty-nine of 100 histologically proved cases of gastric sarcoma were of the lymphoid type. In the remaining 19 per cent, primary sites were widely scattered (see recent report by Parker and Jackson⁹): bone two cases, breast one case, skin of arm one case, lung one case, thymus two cases, prostate two cases, ovary one case, testicle three cases. It is interesting to observe that, though thymic lymphosarcoma is reported rather frequently, only two cases were present in this group. Two thirds of the entire series of patients never had what could reasonably be supposed to represent an extranodal primary focus. In these the first and only subsequent evidence of disease was confined to the node system until widespread dissemination took place. Moreover, many of the patients who have been free from disease for a number of years after receiving treatment to node groups alone never developed an extranodal primary focus which might earlier have remained concealed. It seems logical to suppose therefore that lymphosarcoma is a disease which in the majority of cases begins and

involved, and in 32.4 per cent more than three areas were involved and the disease was considered to be generalized. Only 24 per cent of the patients, therefore, had what might be termed intermediate stages of disease. It is questionable whether patients having three scattered areas of involvement might not be assumed

TABLE 2.—Initial Node Group Involved

Node Group	Right	Left	Bilateral	Total
Cervical.....	21 %	23.6%	12.5%	59.1%
Axillary.....	6.3%	4.5%	0.6%	11.4%
Groin.....	5.1%	5.7%	1.1%	11.9%
Abdomen.....				13.1%
Mediastinum.....				1.1%
Epitrochlear.....				5 %
Generalized.....				2.8%

TABLE 1.—Apparent Extranodal Primary Foci of Disease

Site of Focus	Percentage	Site of Focus	Percentage
Tonsils.....	14	Bone.....	1
Nasopharynx.....	5	Prostate.....	1
Parotid.....	1	Testicle.....	1.5
Antrum.....	1	Ovary.....	0.5
Orbit.....	0.5	Breast.....	0.5
Eyelid.....	0.5	Lung.....	0.5
		Thymus.....	1
		Soft tissue of arm	0.5
Stomach.....	3		
Jejunum.....	1		
Ileum.....	1		
Rectum.....	0.5		
Total cases presenting an extranodal primary focus, 34.5%			

runs its early course in lymph nodes alone. There is certainly no good reason for denying in these structures, the nodes, potentialities generally taken for granted in other mesenchymal derivatives. The site of first node involvement is of considerable interest. In 59 per cent of the cases (table 2) this occurred in the neck (left forty-five, right thirty-seven, bilaterally twenty-two). The axilla was first involved in 11.4 per cent (left eight, right eleven, bilaterally one), the groins in 11.9 per cent (left ten, right nine, bilaterally two), the abdominal nodes in 13.1 per cent, the mediastinum in 1.1 per cent (surprisingly low) and the epitrochlear nodes in 0.5 per cent. In five cases (2.8 per cent) the disease appeared to involve almost the entire node system simultaneously.

Comparable figures for Hodgkin's disease at this hospital indicate the initial sites of node involvement to be neck 68 per cent, axilla 20 per cent, groins 12 per cent, mediastinum and abdomen 0 per cent.¹⁰

Secondary Involvement.—In attempting to arrive at an arbitrary estimate of the extent of disease present on admission, cases were grouped according to the number of areas (not necessarily nodes) clinically involved. Because of recent extirpative surgery, 3.64 per cent had no clinical evidence of disease on admission. In 40.2 per cent there was only one area involved, in 12.5 per cent two contiguous areas contained disease, in 11.4 per cent three areas (not necessarily contiguous) were

to have generalized disease, which, if true, would reduce the intermediate group to 12.5 per cent. In view of only slight differences in the duration of symptoms prior to admission in each of these groups, the smallness of the intermediate group stands as incontrovertible evidence of the rapidity with which the disease advances once it has broken away from the primary site. Indeed, in particular instances untreated disease which had remained apparently static for several years would suddenly or in a few months become widely disseminated.

In general, lymphosarcoma is an acutely malignant disease. Chronic forms do occur but constitute a small minority. In no other disease is metastasis apt to be so sudden and widespread. Hardly an organ or tissue is spared. Lymph node involvement eventually occurs in 100 per cent of cases unless death due to gastric hemorrhage, intestinal obstruction or some unrelated cause suddenly terminates the course of the disease. At first the disease is largely confined to the lymphatic system, contiguous node groups being successively affected; more rarely, widely separate node groups may become involved in rapid sequence or even simultaneously.

In addition to the primary sites of involvement, intra-nodal or extranodal, numerous organs may subsequently become involved either as a result of lymphatic or hematogenous metastasis or by direct extension (table 3).

TABLE 3.—Organs Clinically Involved Later in the Course of the Disease, Presumably as a Result of Hematogenous or Lymphagenous Spread

Site of Involvement	Percentage	Site of Involvement	Percentage
Spleen.....	21	Bladder.....	1.0
Lungs.....	12	Penis.....	0.5
Bones.....	9.7	Ethmoids.....	0.5
Liver.....	8	Brain.....	0.5
Skin.....	5.5	Larynx.....	0.5
Intestinal tract.....	5	Lacrimal gland.....	0.5
Tonsils.....	5	Orbit.....	0.5
Stomach.....	2	Conjunctiva.....	0.5
Testes.....	1.5	Tongue.....	0.5
Spinal cord.....	1.5	Palate.....	0.5
Breast.....	1.0		

The spleen was palpable in 21 per cent of cases, though rarely was it greatly enlarged unless lymphatic leukemia became superimposed. Liver involvement as evidenced by a palpably enlarged organ was noted in only 8 per cent. There was roentgenographic evidence of pleuro-pulmonary infiltration in 12 per cent of cases as manifested by lung mottling or pleural effusion. X-ray evidence¹¹ of secondary bone involvement was present

8. Phillips, J. R., and Kilgore, F. H.: Lymphosarcoma of the Stomach, *Am. J. Surg.* 31: 179 (Jan.) 1936.
9. Parker, Frederic, Jr., and Jackson, Henry, Jr.: Primary Reticulum Cell Sarcoma of Bone, *Surg., Gynec. & Obst.* 68: 45 (Jan.) 1939.

9a. Craver, L. F., and Copeland, M. M.: Lymphosarcoma in Bone, *Arch. Surg.* 28: 809 (May) 1934.

in 9.1 per cent. Undoubtedly this figure is too low. Comparative figures obtained by Anglem for Hodgkin's disease indicate the presence of a palpable spleen in 45 per cent, of a palpably enlarged liver in 24 per cent, of lung involvement in 29 per cent and of bone involvement in 24 per cent. Boring pain, the usual symptom of

breast two, ethmoid sinus one, lacrimal gland one, orbit one, conjunctiva one, palate one, larynx one, bladder two, penis one, spinal cord three, brain one. In cases presenting evidence of hematogenous spread^{9b} (as in lungs, bones, skin and spleen) the prognosis is extremely bad and the life expectancy is apt to be very short. The rapidity with which lymphosarcoma advances is readily understood when one considers that the average duration of life from onset of disease till death was 20.5 months.

Hemogram.—There is no specific hemogram in lymphosarcoma. Early in the course of the disease and for some time after its onset, the blood picture remains amazingly cheering. In contradistinction to patients with Hodgkin's disease, in whom anemia usually develops early (32 per cent on admission), lymphosarcoma patients maintain excellent hemoglobin values for some time (fig. 7). On admission 70 per cent of the patients showed hemoglobin readings above 80 per cent and only 10 per cent of patients less than 70 per cent.

The total white cell count (fig. 8) on admission was above 7,500 in 53 per cent of cases. Twenty-three per cent showed leukocytosis with a count above 10,000.

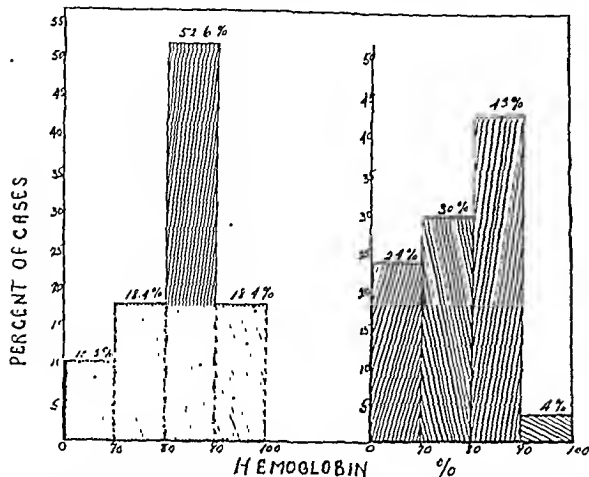


Fig. 7.—The hemoglobin percentage on admission (left) and within six months to one week before death (right).

metastatic bone disease, is far more common in lymphosarcoma than the just mentioned figure of 9.1 per cent would indicate, and many of these patients with bone pain never present any roentgenographic evidence of osseous disease, presumably because the lesion is too small to cast a shadow or because there is insufficient bone reaction to its presence. Treatment becomes mandatory to relieve the pain and usually accomplishes this very nicely, but the possibility of ever obtaining evidence of the disease in the bone may thereby be destroyed. The large bones are more frequently involved (spine, pelvis, skull and long bones) probably because of their proportionately greater blood supply, since secondary lymphosarcoma of bone is largely a manifestation of

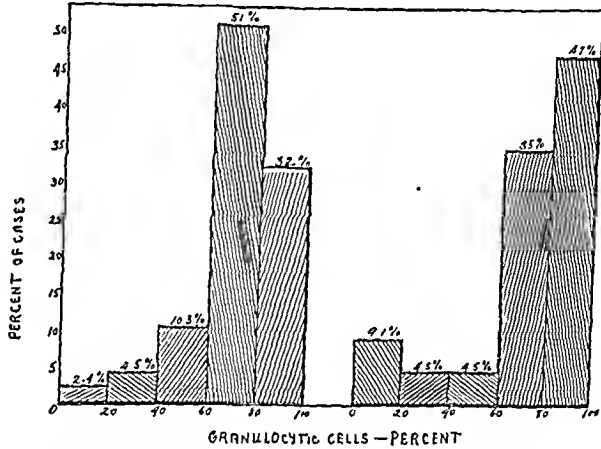


Fig. 9.—Predominance of the granulocytic cells in the blood smear throughout the course of lymphosarcoma; left, on admission; right, six months to one week before death.

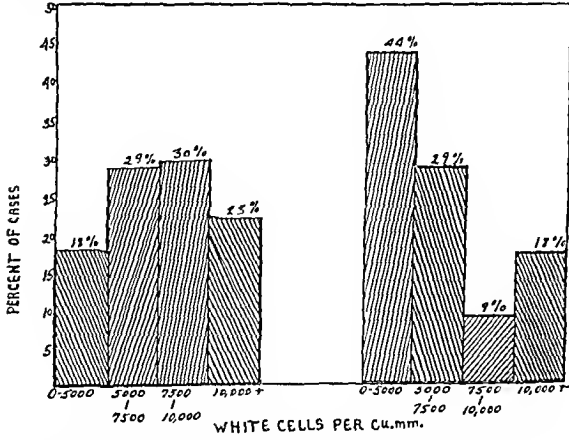


Fig. 8.—A comparison of the total white blood cell count on admission (left) and within six months to one week before death (right).

hematogenous spread. Metastatic involvement of the skin occurs in about 5.5 per cent of cases. Intracutaneous nodules are usually quite firm but lack the hard consistency of carcinomatous nodules and usually have a shiny bluish red appearance. Evidence of presumably secondary gastrointestinal involvement was obtained in 5.5 per cent. In none of these was the duodenum involved. Other organs which later became involved in occasional instances were tonsils five, testis three,

Eighteen per cent had less than 5,000 white cells per cubic millimeter of blood. Cells of the granulocytic series predominated. In 82 per cent of patients (fig. 9) they exceeded 60 per cent and in 31 per cent of the cases the granulocytes exceeded 80 per cent of the total count (definite polycytosis). The lymphocytic cells were, of course, in inverse ratio.

As a result of advancing disease combined with radiation therapy, very definite blood cell changes took place as indicated by counts taken from six months to several days before death. The most important of these changes was anemia. At this time only 46 per cent of cases showed hemoglobin percentages above 80, whereas 24 per cent read less than 70. The total white count dropped to less than 5,000 in 44 per cent and only 27 per cent had more than 7,000 per cubic millimeter. Accompanying this there was little discernible change in the differential count, the granulocytes remaining up. Thirteen patients (6.6 per cent) presented a leukemic or definitely pseudoleukemic blood picture, all of the lymphocytic type.^{9c} Twelve of these had been histo-

9b. Klemperer, Paul: The Spleen in Hodgkin's Disease, Lymphosarcomatosis and Leukemia, *Am. J. M. Sc.* 188: 593 (Nov.) 1934.
9c. Craver, L. F.: Clinical Manifestations and Treatment of Leukemia, *Am. J. Cancer* 26: 124 (Jan.) 1936; Five Year Survivals in Lymphatic Tumors, *Surg., Gynec. & Obst.* 60: 485 (Feb.) 1935; Hodgkin's Disease, Lymphosarcoma and Leukemia, *Laryngoscope* 43: 575 (July) 1933.

logically diagnosed as reticulum cell lymphosarcoma and one as giant follicular lymphoma. In none of the three cases of malignant lymphocytoma was this complication noted.

DIFFERENTIAL DIAGNOSIS

Experience in clinical observation of the lymphomas teaches caution in attempting differential diagnosis except by an excisional biopsy interpreted by a skilled pathologist. In general the best one can do clinically is to hazard a guess, which at times may have to include two, three or more possible diagnoses. There are no clinical features which without exception will permit a differentiation between tuberculous lymphadenitis, Hodgkin's disease, lymphosarcoma, aleukemic lymphatic leukemia, lympho-epithelioma, or even metastatic carcinoma in lymph nodes. The application of a therapeutic test dose of radiation is of little diagnostic value, as any of the first mentioned conditions may respond as readily as does lymphosarcoma.

✓As clinically observed, lymphosarcomas may be roughly divided into two groups: those with a process obviously of monocentric origin, presenting an asymmetrical lymphadenopathy, bulking mainly in one to a few groups of nodes; and those, perhaps of multicentric origin, presenting a fairly uniform symmetrical distribution of nodes, at once suggesting chronic lymphatic leukemia. In the latter group a nonleukemic blood count necessitates a lymph node biopsy to distinguish between generalized Hodgkin's disease, rare cases of metastatic carcinoma, and especially between aleukemic leukemia and lymphosarcoma (if it is proper to make the latter distinction). Moreover, leukemic blood does not necessarily exclude lymphosarcoma. There are also rare cases of generalized symmetrical tuberculous lymphadenitis and other generalized adenopathies of inflammatory or metabolic origin.

Concerning the former more localized types, it may be said in general that lymphosarcoma tends to be more diffuse and more aggressive than the other processes mentioned. The nodes in lymphosarcoma tend to assume a rounded shape and a rubbery firm consistency.

The rare diffuse lymphosarcoma of the nasopharyngeal and oropharyngeal tonsillar ring presents a characteristic appearance. Lymphosarcoma of the tonsil, when fully developed, usually presents a bulky smooth spongy swelling in the tonsillar fossa with little or no ulceration until late stages. Lymphosarcoma of the stomach, like lymphatic leukemia, may produce giant rugae. In the intestine, lymphosarcoma may produce a bulky palpable mass with comparatively little stenosis of the lumen. In the skin, lymphosarcoma characteristically causes raised, dusky red button-like plaques, similar to leukemia cutis.

(To be continued)

Education of Adult Blind.—In the United States there are 27,872 blind persons between the ages of 25 and 64 years, and 28,113 of over 64 years, according to the 1930 federal census. The National Health Survey of 1935-1936 estimates that there are 76,000 blind persons of over 55 years of age, 33,000 of between 25 and 55 years. The average age of the blind is just over 60 years; 78.7 per cent of the blind are over 45 years of age. Only 45.9 per cent of these blind persons have ever attended school. . . . About 8,000 blind persons in the United States are taught by home teachers, and there is an average of one teacher to every 100 persons taught.—Education of the Handicapped, edited by M. E. Frampton and H. G. Rowell, Yonkers-on-Hudson, New York, 1940, vol. 2, p. 150.

ORAL POLLEN THERAPY IN RAGWEED POLLINOSIS

A COOPERATIVE STUDY

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The progress made in the last few years in the various phases of immunotherapy has stimulated the search for more simple methods for the administration of such treatment. Attempts at substitution of the oral method for the hypodermic type in vaccine and allergen administration were begun many years ago. Among the first clinical conditions for which prophylaxis by ingestion was suggested is hay fever. The hope of safety, convenience, inexpensiveness and painlessness of the oral method has been the motivating factor stimulating this idea.

In 1900, more than ten years prior to the advocacy of hypodermic pollen therapy, Curtis¹ had recommended the oral administration of extracts of ragweed pollen. He had previously observed the good effects of infusions of roses and other flowers in those sensitive to them. The patients were given, three times daily after each meal, from 2 to 10 drops of a tincture or infusion of the flowers and pollen of ragweed. For most patients the treatment was begun two weeks prior to the season and continued through the season. For some it was used coseasonally only. With both methods of treatment good results were obtained in the majority of cases.

Strangely enough, for the next twenty years or more, the possibilities inherent in such therapy seemed to have been ignored. In 1922 Touart² described the results that were obtained from treating six patients with daily doses of 0.1 mg. pollen tablets coated with phenyl salicylate. The grass-sensitive patient obtained relief, while only one of those allergic to ragweed pollen was benefited.

Black in 1927³ and 1928⁴ reported on his results with oral pollen therapy. While he obtained complete failures in 6 per cent of hay fever cases treated hypodermically, the failures with the oral method amounted to 20 per cent. In the cases of pollen asthma, complete failures resulted in 22.2 per cent with oral treatment, while with the hypodermic method no complete failures occurred. Thommen⁵ has reported the successful oral

The pollen and placebo capsules for this study were obtained through Eli Lilly & Co., Indianapolis. This product has not been considered by the Council on Pharmacy and Chemistry of the American Medical Association.

1. Curtis, H. H.: The Immunizing Cure of Hay Fever, M. News, New York 77: 16, 1900.

2. Touart, M. D.: Hay Fever: Desensitization by Ingestion of Pollen Proteins, New York M. J. 116: 199 (Aug. 16) 1922.

3. Black, J. H.: The Oral Administration of Pollen, J. Lab. & Clin. Med. 12: 1156 (Sept.) 1927.

4. Black, J. H.: The Oral Administration of Pollen: A Clinical Report, J. Lab. & Clin. Med. 13: 709 (May) 1928.

5. Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, Publisher, 1931, p. 764.

pollen treatment of one hay fever patient, but his experiences with later cases were disappointing. Urbach⁶ for a number of years has been advocating specific oral pollen peptone therapy.

Gatterdam⁷ in 1933 and 1934 recommended this type of treatment on the basis of his report, describing good results in from 75 to 85 per cent of a series of eighty-five patients. The author administered from 3 to 15 drops of a 3 per cent pollen extract twice daily, with additional doses during attacks. The pollens employed were those of cottonwood, ash, Bermuda grass, rabbit bush and false ragweeds. McGrew⁸ tried oral pollen therapy on the basis that he had known some hay fever sufferers to claim relief by the ingestion of honey and that the pollen in the honey might be responsible for this action. Coscason treatment was given, using from 1 to 10 drops of a 1 per cent extract three times daily for the immediate relief of an individual attack. Of thirty-three patients, twenty-nine were improved. Those having asthma did not do as well.

Despite the reports just cited, it was not until the work of Stier and Hollister⁹ became known that this subject began to arouse general interest. In an experience extending over three years these authors obtained satisfactory results in 78 per cent of a large series of hay fever cases. Their best results were obtained with the coseasonal method. The doses varied from 3 drops of a 1:100,000 dilution to a maximum dose of 21 drops of a 1:100 dilution (from 2 to 14,000 pollen units). A large variety of pollen was used but, because their region does not contain ragweed, it did not include an evaluation of oral ragweed therapy.

Rockwell¹⁰ in 1938 reported on his results in a series of hay fever cases treated during the years from 1935 to 1937 inclusive. His methods differed somewhat each year, but his latest method was the use of dry ground pollen in capsules. Beginning with 500 pollen units (0.5 mg.) the doses were increased to 120,000 or 240,000 (120 to 240 mg.). Preseasonal doses were given twice weekly and the seasonal doses several times weekly. In coseasonal treatment the capsules were given three times daily at first. The coseasonal therapy yielded the best results, satisfactory relief occurring in 75 per cent of his cases.

Bohner,¹¹ employing the same technic as Rockwell, obtained less happy results. Of twenty-one patients, thirteen obtained satisfactory benefit while of an equal number treated hypodermically sixteen were benefited. In the same year Bernstein and Feinberg¹² analyzed the results in twenty ragweed-sensitive patients treated with pollen orally during the 1937 season. Pollen extract, well diluted, in doses from 6,000 to 180,000

pollen units, were administered daily. All patients were treated coseasonally. Only two obtained some degree of relief.

Recently Black¹³ reported a reinvestigation of the oral method during the 1938 season in Dallas. Of forty patients treated with daily doses of 500 to 4,000 units, sixteen (40 per cent) obtained satisfactory relief. Black makes the observation that in some instances oral pollen therapy was of aid as adjunct treatment in overcoming the tendency of the individual to repeated systemic reactions from the hypodermic injection of the extract. London¹⁴ investigated the combined effect of hypodermic and oral pollen therapy. He concludes that patients adequately treated by the subcutaneous method can expect no further benefit from the supplementary oral administration of pollen.

Of twenty-two ragweed patients treated preseasonally by Zeller¹⁵ during 1938 with pollen given orally, 20 per cent obtained good results. Of the five who obtained good results two had had from three to four years of good results previously with hypodermic therapy. The simultaneous administration of the oral pollen and hypodermic treatment did not improve the results of the latter treatment. In the discussion of Zeller's paper,¹⁵ Vaughan mentioned that he obtained relief by the oral method in from 10 to 20 per cent of his cases. Ellis obtained complete failures in fourteen out of fifteen cases. Bernton recalled that fifteen years previously he treated thirty hay fever patients with pollen tablets with complete failure in all. Bohner cited statistics less favorable than he had reported previously.

Most of the papers report a fairly high incidence of gastrointestinal reactions. For instance, Bernstein and Feinberg¹² report an incidence of 30 per cent, Zeller¹⁵ an incidence of over 40 per cent. There is much less certainty concerning constitutional allergic reactions such as urticaria, hay fever or asthma. If they occur they are uncommon. This observation provokes the question of absorption of the pollen administered orally. Black³ found that the ragweed atopen could be demonstrated in the blood and urine after the ingestion of large amounts of pollen extract. The basis for his conclusion was the observation of positive intra-antennous tests with such blood serum in ragweed-sensitive persons and in those passively sensitized. Clarence Bernstein Jr. and Kirsner¹⁶ were unable to demonstrate enteral absorption from a 0.3 Gm. capsule of ragweed pollen sufficient to cause a reaction in passively sensitized sites in four persons. Using similar methods T. B. Bernstein and Feinberg¹² tested enteral absorption of ragweed pollen in seventeen nonallergic subjects. In sixteen no reactions were obtained, although doses as high as 5 Gm. (5,000,000 pollen units) were administered. In one person with a bleeding carcinoma of the stomach, evidence of absorption was obtained. It is interesting to note that in all of these seventeen persons the hypodermic administration of pollen extract showed reactions in the distantly sensitized sites with amounts as little as one five-thousandth part of that used orally. Zeller¹⁵ and London¹⁴ independently confirmed these observations by employing a combination of the methods used by Bernstein and Feinberg with those of Black.

6. Urbach, Erich: "Die Behandlung allergischer Individuen auf oralem Wege mit Pollen-Extrakt," *Wochenschr.* 10: 534 (March 21) 1937.

7. Gatterdam, E. A.: "Oral Administration of Pollen Extracts, Southwest Med." 17: 199 (June) 1933; "Hay Fever in Central Arizona and Its Treatment with Oral Extracts," *ibid.* 18: 130 (April) 1934.

8. McGrew, G. D.: "Time and Money Saved in the Treatment of Hay Fever," *Mil. Surgeon* 80: 371 (May) 1937.

9. Stier, R. F. E., and Hollister, Guy: "Desensitization by Oral Administration of Pollen Extracts," *Northwest Med.* 36: 166 (May) 1937.

10. Rockwell, G. E.: "Clinical Results in the Prevention and Treatment of Hay Fever by Oral Administration of Pollens of the Grass and Ragweed Types," *Ohio State M. J.* 34: 784 (July) 1938.

11. Bohner, C. B.: "Treatment of Ragweed Pollinosis: Comparison of Oral and Hypodermic Medication," *J. Indiana M. A.* 31: 279 (June) 1938.

12. Bernstein, T. B., and Feinberg, S. M.: "Oral Ragweed Pollen Therapy: Clinical Results and Experiments on Gastrointestinal Absorption," *Arch. Int. Med.* 62: 297 (Aug.) 1938.

13. Black, J. H.: "The Oral Administration of Ragweed Pollen," *J. Allergy* 10: 156 (Jan.) 1939.

14. London, McKinley: "Combined Oral and Subcutaneous Treatment for Ragweed Pollinosis," *J. Allergy* 10: 453 (July) 1939.

15. Zeller, Michael: "Oral Ragweed Pollen Therapy (with discussion)," *J. Allergy* 10: 579 (Sept.) 1939.

16. Bernstein, Clarence, Jr., and Kirsner, J. B.: "Oral Pollen Therapy," *J. Allergy* 8: 221 (March) 1937.

The somewhat conflicting results of the published reports and the potential importance of such a method of therapy stimulated several of us connected with the allergy clinics at the University of Illinois College of Medicine, Northwestern University Medical School, Rush Medical College, University of Chicago and the University of Michigan Medical School to plan a cooperative project in the summer of 1939, in order to evaluate oral pollen therapy. It was planned that the several institutions would proceed with their own work and observations with slight individual variations, but that each would follow the same general plan herein described.

The patients selected were those who had ragweed hay fever or hay fever and asthma and either had never been treated hypodermically or at least had had no treatment later than 1937. This was done to eliminate the possible residual benefit obtained from previous hypodermic therapy. The materials administered to the patients were capsules containing differing amounts of dry pollen diluted with starch. The capsules of varying content were of different colors for the sake of identification. Identically colored capsules containing starch only were available for placebo purposes. The majority of the patients selected for the experiment received the pollen capsules together with an injection of physiologic solution of sodium chloride.

Those treated preseasonally were instructed to take single doses twice weekly, beginning with 500 pollen units and doubling each dose until the level of about 180,000 units was reached. When patients reported after mid-July the intervals were shortened in order to reach the maximum dose before August 15. During the season instructions were given to take the capsules once daily. A few divided their daily portions into two or three doses. Those who began their treatment during the season were instructed to take the pollen three times daily. The capsules were usually administered after meals.

Before treatment was started, all the investigators used a uniform questionnaire eliciting specific data as to the severity and character of each patient's past seasons, especially the 1938 season as the one most recently in memory. The information thus obtained was the yardstick for comparison of results in the 1939 season.

After pollination began the patients were questioned and observed as to the frequency and severity of symptoms, and written notations were made. Every attempt was made to elicit objective data, such as loss of sleep and interruption of work, as well as the patient's own estimate of symptoms. Discrepancies between the patient's report and our own observations were usually reconciled by a cross examination of the patient or his relatives. If the patient failed to report weekly, the social service department investigated by telephone or letter; this cooperation made a very complete follow-up study possible.

RAGWEED ORAL POLLEN THERAPY COMPARED WITH ORAL PLACEBO¹⁷

BY DRs. BEN Z. RAPAPORT, MICHAEL ZELLER
AND EMANUEL PADNOS

The main group in this study consisted of 103 subjects varying in age from 6 to 73 years. Fifteen of these were children under 14 years. Sixty-four had

uncomplicated autumnal hay fever, while thirty-nine had fall pollen asthma. (In addition to this group of 103, one of us [E. P.] studied twelve children, whose cases will be discussed under a separate heading.) All had positive cutaneous reactions to the ragweed pollens. Seventy-one of the group, consisting of the thirty-nine patients with asthma and thirty-two with hay fever, were given ragweed pollen orally. The remaining thirty-two, all with uncomplicated hay fever, were given placebo capsules which were identical in color and appearance with the oral pollen capsules. It was not considered justifiable to include patients with asthma in the placebo group. In addition to the pollen or placebo capsules, each patient received a subcutaneous injection of physiologic solution of sodium chloride on reporting to the clinic once a week.

DOSAGE

The initial oral dose of ragweed pollen varied from 1,000 to 2,000 units. This dose was increased by doubling the previous dose twice a week for those patients who reported early for treatment. Only eight of the patients came after July 1. The dose in this small group was given more frequently to attain a comparable maximum pollen dose. The maximum dose attained was 60,000 units by thirteen patients, 120,000 units by thirty-three, 180,000 units by nineteen and 240,000 units by two. This was attained with no untoward symptoms by thirty-six of the seventy-one patients several weeks before the onset of the hay fever symptoms. It was maintained at the level planned in spite of the fact that an increase in dose could easily have been given to most of the patients. With the onset of symptoms during the first ten days of August the maximum preseasonal dose was given daily. It was, however, varied from day to day, being increased in most cases in an attempt to control symptoms.

The total amount of pollen ingested during the course of treatment varied even more than the maximum dosage. Three patients received between 1 and 2 million Noon units, twenty-six between 2 and 4 million, nine between 4 and 6 million, nineteen between 6 and 10 million, twenty-two between 10 and 15 million and two patients more than 15 million.

UNTOWARD EFFECTS OF ORAL POLLEN

The untoward effects of treatment consisted principally of gastrointestinal symptoms such as abdominal cramps, nausea, vomiting and diarrhea. In some patients these symptoms manifested themselves after each individual dose, while in others they developed at irregular intervals without any apparent relationship to dosage. Gastrointestinal symptoms were usually noted within one half hour to two hours after ingestion of the capsules and persisted for periods varying from one to thirty-six hours. In some instances reduction of dosage or abstinence from oral pollen apparently increased gastrointestinal tolerance to a point where continued treatment was possible without untoward reactions.

Four patients started on oral therapy and not included in the group of 103 previously discussed had violent abdominal pain and diarrhea and refused further treatment before the onset of the hay fever season.

Hay fever after oral pollen occurred in eleven cases, but in no instance was it severe, and it usually subsided within one hour. Other possible sources of nasal symptoms were ruled out before considering oral pollen as

17. From the Allergy Clinic of the Departments of Medicine and Pediatrics, University of Illinois College of Medicine.

the cause. In one case asthma followed the initial oral pollen dose on repeated trials. Further therapy was, therefore, not practical. In one other instance asthma occurred several times after ingestion of 120,000 units, but on reduction of the dose further difficulty was avoided. Three patients had headache, drowsiness and dizziness. Urticaria was not observed in any instance.

These observations as well as those to be discussed in the reports of our collaborators indicate that the majority of the untoward reactions are limited to the gastrointestinal tract. The effect of a large initial dose, however, produced no untoward effect in any of the patients to whom it was given. Five of the patients who had asthma were given 30,000 ragweed pollen units one hour after a heavy meal as the initial pre-seasonal dose. No gastrointestinal or other symptoms followed this. Ten of the thirty-two patients placed on placebo treatment were likewise given a large initial dose of ragweed pollen before receiving the placebo capsules. Five of the ten were given 30,000 pollen units

TABLE 1.—Summary and Comparison of Results in 103 Ragweed-Sensitive Patients Treated by Oral Pollen and by Oral Placebo at the University of Illinois College of Medicine

	Un-Improved	Improved	Degree of Improvement				Excellent
			Slight	Moderate	Good		
Asthma (oral pollen)....	33 (82%)	7 (18%)	0	5 (12.8%)	2 (5.2%)		0
Hay fever (oral pollen)....	20 (62.5%)	12 (37.5%)	0 (18.75%)	3 (9.37%)	3 (9.37%)		0
Hay fever (oral placebo)...	25 (78.1%)	7 (21.9%)	1 (3.1%)	4 (12.5%)	0		2 (6.25%)

while the other five received 60,000 pollen units. No gastrointestinal or other symptoms occurred in any of these patients.

RESULTS

The results of treatment are briefly indicated in table 1. In more detailed protocols attempts were made to determine whether improvement in each case was slight, moderate, good or excellent. These have been condensed in table 1.

It will be noted that of the thirty-two patients with uncomplicated hay fever twenty (62 per cent) showed no improvement. Six were slightly improved and six showed moderate (50 per cent) to good (75 per cent) improvement.

The thirty-nine asthma patients may be grouped into two classes, thirty-two (82 per cent) with no improvement and seven (18 per cent) with moderate to good results. None were completely or nearly completely relieved. Of the thirty-two who were unimproved, five had asthma as severe as in the previous untreated year while fourteen stated that their condition was worse.

Fifteen of this group of 103 patients were children aged 6 to 14. Seven of the fifteen had autumnal asthma; none of these showed any improvement. Eight of the fifteen had simple autumnal hay fever; six were unimproved while two had slight improvement. Three of these fifteen had a maximum oral pollen dose of 60,000 units. The rest reached a dose of from 120,000 to 180,000 units. These patients were studied by two of us (B. Z. R. and M. Z.).

A group of twelve children ranging in age from 7 to 15 years was studied separately by one of us (E. P.). The results in this group were so different that the subjects are described separately and were not included among the 103 patients previously discussed. Nine of these patients had simple autumnal hay fever, while three had autumnal asthma. Eleven of the twelve received ragweed pollen orally while the twelfth received placebo capsules. Five other placebo-treated patients of the group discontinued treatment before the beginning of the hay fever season. The maximum dose attained was 120,000 pollen units by one, 180,000 units by three, 240,000 units by one, 360,000 units by three and 420,000 units by three. No untoward symptoms occurred in any of the patients.

The parents as well as the children were questioned regarding the results obtained. Eight of the nine hay fever patients receiving oral pollen claimed improvement—with the following estimates of the degree of relief: one very slight, two moderate, four good and one excellent. The three patients with autumnal asthma were all moderately improved. The one patient receiving placebo capsules was also moderately improved. According to the results obtained in this group, all patients, the three with asthma and the nine with hay fever, including the one patient receiving placebo therapy, had moderate to marked improvement.

PLACEBO GROUP

The surprise of the experiment came in tabulating the results of the oral placebo group. Great care had been taken to treat and question these thirty-two patients in the same manner as those receiving pollen orally. Seven of the group (21.9 per cent) stated that they were improved, while twenty-five (78.1 per cent) were unimproved. Of the seven who were improved by the placebo capsules and saline injections, six (85.7 per cent) had more than moderate relief. Two of these six had results classified as excellent, an apparently better result than that obtained by any of the patients receiving oral pollen therapy.

COMMENT

The interesting comparison in this study is in the results of the thirty-two patients with simple hay fever given pollen orally and the equal number given placebo capsules orally. Of those receiving pollen orally, six were slightly improved and six had moderate to good results. In the oral placebo group only one was slightly improved, while six had moderate to excellent results. The similarity of these results is striking. Unfortunately, the number of patients in both groups is too small for any definite conclusions to be drawn.

On the other hand, when one compares the results obtained in the two groups of children studied, no good explanation can be offered for the discrepancies shown. In the fifteen patients under 14 years studied by two of us (B. Z. R. and M. Z.) only two had slight improvement. All of the twelve children studied by one of us (E. P.), including the one given a placebo, reported improvement. This report was confirmed by the parents. Only one of this uniformly favorable group reported slight (questionable) improvement. It will be noted that seven of the eleven in this latter group received a maximum dose of from 240,000 to 420,000 pollen units. This is definitely a much higher dose than that received by the other group of fifteen children. We are uncertain whether this accounts for the difference in results reported or whether it is largely a difference of interpretation by different observers.

SUMMARY

1. In this study, thirty-two patients with uncomplicated ragweed hay fever were given pollen orally, while an equal number received placebo capsules.

2. Of the thirty-nine patients with asthma who received pollen orally, seven (18 per cent) stated that they had moderate to good results. None were completely relieved. The remainder (82 per cent) were unimproved. Of the thirty-two patients with uncomplicated hay fever receiving pollen orally, six (18.75 per cent) were slightly improved and six (18.75 per cent) had moderate to good results; of the thirty-two receiving placebo capsules orally, one (3.1 per cent) was slightly improved while six (18.75 per cent) had moderate to excellent results. Therefore the results for subjects with uncomplicated hay fever treated with oral pollen show no substantial difference from results for those receiving placebo capsules.

3. Two groups of children studied by different observers show conflicting results. In one group, eleven patients receiving oral pollen reported uniformly favorable results. In the other group of fifteen receiving oral pollen, only two reported slight improvement.

COMPARISON OF ORAL POLLEN WITH
PARENTERAL POLLEN IN THE
TREATMENT OF RAGWEED
POLLINOSIS¹⁸

By DRS. FRANCIS L. FORAN AND
MEYER R. LICHTENSTEIN

Two groups were observed in this series, each reporting to the clinic on an average of once a week. The "oral pollen group" of thirty-two patients received on each visit an injection of physiologic solution of sodium chloride and a sufficient number of pollen capsules with a written dosage schedule for the ensuing week. The "parenteral pollen group" of twenty-five patients received on each visit an injection of pollen extract and a number of placebo capsules, also with written directions and dosages for the ensuing week.

None of the fifty-seven patients used in this study had received treatment in 1938. Of the oral group eleven had received parenteral injections in some years previous to 1938; of the parenteral group six had received such treatment previous to 1938. Only two patients in the entire series were under 16 years of age; otherwise the ages ranged from 16 to 72.

Throughout the study care was taken to make the same inquiries of both groups as to symptoms and reactions in order to equalize as far as possible the psychologic factors. Thus patients of both groups were asked in a routine way about local reactions from the injections. The saline injections occasionally gave slight discomfort, enough to rationalize the inquiry to the patient receiving them. Again, to avoid leading questions, we made no inquiry about gastrointestinal reactions until a complaint was volunteered.

TREATMENT AND DOSAGE

Treatment was begun during May in all but six cases and continued into the first week of September or later with only two exceptions, the two subjects refusing further treatment because of severe gastrointestinal reactions.

The range of dosage is summarized in table 2, items D, E and F. In averaging the number of doses and the maximum daily dose the entire daily intake is

counted as one dose, although many patients split the amount into two or more fractions, usually because of gastrointestinal discomfort with the larger amount. The total course dose is the sum expressed in Noon units of all the pollen ingested or injected during the entire course of treatment.

It is pertinent to compare the ratio of doses used in the two groups. The average maximum daily dose of the oral pollen was approximately fifty times that of the parenteral pollen extract (table 2, item E) and the average total pollen ingested throughout the entire course of treatment was approximately two hundred times that injected in the parenteral group (table 2, item F).

REACTIONS

Eight (25 per cent) of the oral group had gastrointestinal reactions such as epigastric pain, cramps, nausea, vomiting or diarrhea. In three patients the

TABLE 2.—Summary of Study of Oral Pollen Therapy.
Rush Medical College, University of Chicago

Type of Cases	Oral Group *	Parenteral Group †
A. Total number of cases.....	32	25
B. In 1938, hay fever only.....	15	10
C. In 1938, hay fever and asthma...	14	15
	(44% of A)	(60% of A)
Treatment in 1939 Season		
D. Average number of doses.....	40	14.4
Variation.....	(23-62)	(7-21)
E. Average maximum daily dose....	116,000	2,452
Variation.....	(60,000-120,000)	(700-4,500)
F. Average total course dose.....	3,237,000	16,517
Variation.....	(673,000-5,113,000)	(1,930-41,320)
Results of Treatment		
G. In 1939, hay fever only.....	10	10
H. In 1939, hay fever and asthma....	22	15
	(69% of A)	(60% of A)
I. In 1939, asthma for first time....	9	2
	(30% of B)	(20% of B)
Comparison with 1938 Season		
J. Symptoms same	3 (10%)	7 (28%)
K. Symptoms better	8 (25%)	14 (56%)
L. Symptoms worse	21 (65%)	4 (16%)

* Received oral pollen and saline injections.
† Received pollen extract injections and placebo capsules.

symptoms were of repeated occurrence and one of them finally refused further treatment on August 26. Still another, a medical student, discontinued treatment on August 26 after severe nausea and diarrhea, although the pollen had been fairly well tolerated to that time. The other patients with gastrointestinal symptoms were readily relieved by reducing or fractionating the dose.

Two patients complained of urticaria and two of pruritus, both symptoms being of minor severity and of brief duration. One patient only spoke of "choking" after 90,000 units, but no definite asthma syndrome seemed to have occurred.

No systemic reactions occurred in the parenterally treated group, owing probably to the conservative dosage schedule followed.

RESULTS

It should be remarked that the 1939 season was more severe in the Chicago area than that of 1938 and therefore the mere fact of aggravation of symptoms does not preclude some effectiveness of the therapeutic agent employed. However, a comparative estimate of the experimental and control groups is a fair and reasonable ground for conclusions.

18. From the Allergy Clinic, Rush Medical College, University of Chicago.

The characterization of results as "same," "better" or "worse" (table 2, items J, K and L) is an attempted correlation of the entire 1939 pollinosis syndrome as described by the patient and observed by us in comparison with the symptoms of the 1938 season. It is our impression that the clinical differences in the two groups were much wider than the statistical percentages indicate. Thus the level of improvement in the "better" patients of the parenteral group is higher than the approximate 2 to 1 ratio conveys; and, on the other hand, "worse" includes severe aggravation of symptoms in several patients of the oral group but in none of the parenteral group.

An observation of particular note is the increased incidence of asthma (table 2, item H) during the 1939 season in the oral group as compared with the control group: an increase of 25 per cent in the former while the latter remained stationary. This is made further evident by the observation (table 2, item I) that 50

TABLE 3.—Correlation of Results with the Maximum Pollen Dose in Thousands of Noon Units

Maximum Daily Pollen Dose, Units	Not Improved	Im- proved	Total Number Patients	Degree of Improvement			
				Slight	Mod- erate	Good	Excell- ent
50 thousand..	2	0	2	0	0	0	0
60 thousand..	13	4	17	0	2	2	0
		23.6%			11.8%	11.8%	
80 thousand..	3	1	4	0	1	0	0
		25%			25%		
120 thousand..	45	10	55	0	5	7	1
		36%		0.4%	7.8%	10.0%	1.6%
180 thousand..	20	8	28	1	5	2	0
		21.6%		2.7%	13.5%	5.4%	
210 thousand..	3	2	5	1	0	0	1
		40%		20%			20%
210+ thousand	4	8	12	1	6	1	0
		66.7%		8.3%	50%	8.3%	
Totals.....	89	42	131	0	10	12	2
		29.8%		0.4%	13.5%	8.5%	1.4%

Percentages are in terms of the total number of patients in the same horizontal.

per cent of the "hay fever only" patients in the oral group had asthma for the first time in 1939 as compared with 20 per cent in the parenteral group.

COMMENT

In this comparison of two therapeutic procedures we conclude that parenteral treatment with pollen extract was definitely more effective than oral ingestion of pollen, despite an enormous preponderance of dosage in the latter.

However, the 25 per cent of improved cases in the oral group cannot be dismissed as of no significance on the evidence of this series alone. If we are to charge these apparent improvements to chance variations in exposure or susceptibility or to the influence of mental suggestion, a like restriction must be put on all reports of pollen therapy.

SUMMARY

1. The results of treatment of thirty-two patients with ragweed pollinosis by the oral ingestion of pollen were definitely inferior to those of a control group of twenty-five patients treated by the subcutaneous injection of pollen extract.

2. Of those treated orally 25 per cent reported improvement compared with 56 per cent of those treated parenterally.

3. Severe gastrointestinal symptoms occurred in 12.5 per cent of the oral pollen cases and minor gastrointestinal discomfort in another 12.5 per cent.

4. No asthmatic or anaphylactoid symptoms occurred.

RESULTS OF ORAL POLLEN THERAPY¹⁰

By Drs. SAMUEL M. FEINBERG AND JOHN SHELTON

In these clinics twenty-seven patients received oral pollen therapy, all except one also receiving placebo injections. None were given oral placebos. There were eleven males and sixteen females. The ages ranged from 8 to 74 years, and only two children were included. Of the group twelve had asthma with their hay fever. Ten had hypodermic treatment for one to two years prior to 1938, with satisfactory results in nine. The others had never had pollen injections. The method of administration was as outlined in the introduction, the maximum daily dose being 30,000 Noon or pollen units in two cases, 90,000 units in two, 120,000 units in one, 180,000 units in fifteen, 240,000 units in two, 270,000 units in three, 360,000 units in one and 540,000 units in one. The total ingestion for the entire period was from about 0.2 to 10 million units in the majority of instances, one patient receiving as much as 25,000,000 units (25 Gm.).

In twelve cases there were gastrointestinal reactions, ranging from slight discomfort and gaseous distention to nausea, abdominal pain and diarrhea. The doses causing the reactions were usually small, and with increasing doses the symptoms disappeared in the majority. This may be regarded, perhaps, as preliminary evidence of a decrease in the local allergy. In two patients there were one or two mild attacks of hay fever and asthma. It is not at all certain, however, that these were constitutional reactions since these individuals were susceptible to minor attacks of respiratory allergy out of season.

In twenty-three of our patients no indication of benefit was observed. In one patient the hay fever was slightly benefited while in another it was moderately benefited. Of two patients with hay fever and asthma the former appeared to be definitely improved although the asthma remained as in previous seasons. It appears, then, that in this group of patients several showed some relief from the nasal symptoms but none obtained relief from the asthma. Since asthma is almost always a later manifestation in the progress of pollinosis and since in hypodermic therapy the relief obtained from the asthma is more certain and is apt to occur before the relief of hay fever, it would appear that more reliance can be based on asthmatic symptoms in evaluating the results. Our present observations corroborate our past experiences and strengthen the impression that the value of oral pollen therapy is questionable.

GENERAL DISCUSSION

Under the circumstances of this study, in which there have been several groups of investigators working independently in different clinics, a considerable variation in results was to be anticipated.

Such variation is found in the extremes represented by the reported improvement of 100 per cent of the small pediatric series observed by one of us (E. P.) in contrast to the 14.8 per cent of the Northwestern-Michigan series. On the other hand, the statistics of

19. From the Allergy Division, Department of Medicine, Northwestern University Medical School, and the Allergy Division, Department of Medicine, University of Michigan Medical School.

the three larger groups show a much closer approximation, the improvement reported in the main Illinois series occurring in 26.8 per cent of seventy-one patients; in the Rush series, 25 per cent of thirty-two patients, and in the Northwestern-Michigan series, 14.8 per cent of twenty-seven patients. The pooled results of all the clinics presented in tables 3 and 4 yield the fact that in 29.8 per cent of 141 cases there was an apparent improvement under oral pollen therapy.

That this percentage is more impressive in the statistics than it was in the clinics is made apparent by the further breakdown of the figures into degrees of improvement. From these it appears that only two (1.4 per cent) of the 141 patients obtained "excellent" results; that twelve (8.5 per cent) obtained "good" results, and that the remaining twenty-eight (19.9 per cent) were in the columns indicating "slight" to "moderate" improvement.

Moreover it was in the relief of asthma, the touchstone of pollen therapy, that the oral treatment showed to least advantage. In the main Illinois series only 18 per cent of the asthma patients showed improvement compared with 37.5 per cent of the patients with uncomplicated hay fever—a reversal of the common experience with the injection method of treatment. In the Northwestern-Michigan series, of the twelve asthma patients none showed relief of the asthma, although two had some abatement of the nasal symptoms. In the Rush series there was a 25 per cent increase in the incidence of asthma in comparison with the season in which no treatment was given, owing to the fact that 50 per cent of the patients with the previously uncomplicated hay fever contracted asthma for the first time in 1939.

Controls.—Extended comment on the parenteral control series is unnecessary. Its purpose was to provide a treated control group, comparable in season, duration of treatment, type and selection of patient. Its results are somewhat less favorable than general experience with this mode of therapy but sharply superior to those of the companion oral group.

The placebo control group furnished surprising statistics. The 21.9 percentage of improvement in the thirty-two cases in which placebo capsules were received (table 1) approximates the 29.8 per cent of improvement noted in the combined group given oral pollen (tables 3 and 4). This becomes more striking in that two (6.25 per cent) of the patients receiving the starch capsules reported "excellent" relief compared with only 1.4 per cent of those treated with pollen capsules.

The implications of these data are apparent and challenging. At the very least, the placebo report detracts substantially from the significance of the percentages of improvement with oral pollen, if it does not wholly nullify it. We recognize also that the figures impinge proportionately on the control parenteral group and indeed on all reports of pollen therapy. We have here one more example of the need of caution in interpreting results based, however necessarily, on clinical impressions in the absence of sharply defined objective criteria.

Reactions.—Reactions of an untoward nature were mainly gastrointestinal. These occurred in 33 per cent of the combined series and, while severe in some instances, were for the greater part readily controllable by fractionating the dose.

Preseasonal attacks of hay fever were noted during the course of oral treatment in eleven (7.8 per cent)

patients and asthma, either alone or in association with other symptoms, in five patients (3.6 per cent) of the combined series. Whether or not there were instances of systemic reactions was not wholly determinable. The failure by one of us (B. Z. R.) to elicit such reactions by the ingestion of large initial doses of pollen would be evidence against absorption to the point of systemic reaction.

Dosage.—Tables 3 and 4 present the range of dosage in relation to the spread of improvement. No definite conclusions seem warrantable.

In table 4 it is obvious that the results did not follow in direct proportion to the mass of dosage. The 6 to 10 million unit group of twenty-eight patients and the 10 to 15 million unit group of twenty-six are comparable numerically, but the percentage of improvement in the former is double that in the latter. If any inference can be made it is that the optimum mass dose lies between 4 and 10 million Noon units of ingested pollen.

TABLE 4.—Correlation of Results with Total Amount of Pollen Ingested in Millions of Noon Units

Total Pollen Ingested, Units	Not Improved	Im. proved	Total Number Patients	Degree of Improvement			
				Slight	Moderate	Good	Excellent
0.5-1 million...	4	0	4	0	0	0	0
1-2 million....	9	0	9	0	0	0	0
2-4 million.....	26	15 29.4%	51	4 7.8%	6 12%	4 7.8%	1 2%
4-6 million.....	12	8 40%	20	2 10%	2 10%	4 20%	0
6-10 million....	15	13 46.8%	28	3 10.7%	6 21.4%	4 14.3%	0
10-15 million....	20	6 23%	26	0	5 19.2%	0	1 3.8%
15-30 million....	3	0	3	0	0	0	0
Totals.....	99	42 29.8%	141	9 6.4%	19 13.5%	12 8.5%	2 1.4%

Percentages are in terms of the total number of patients in the same horizontal.

The table of maximum daily doses (table 3) is heavily weighted by the exceptional results of the small pediatric series. Seven of the twelve patients receiving in excess of 240,000 units were members of that group. Here again results bear no consistent relation to dosage. It is true that the highest percentages are seen with the highest maximum dosage, but their statistical significance is greatly impaired by the relative paucity of cases in these groups. In the two largest groups of cases, the 120,000 unit maximum dose shows to slight advantage over the 180,000 unit dose.

CONCLUSIONS

1. In our appraisal of oral pollen therapy on the basis of our combined results the opinions of the investigators diverge from a complete rejection to a limited acceptance.

2. We concur in the opinion that the oral ingestion of pollen, in the doses used in this inquiry, is a safe procedure; that gastrointestinal reactions are frequent and troublesome, sometimes severe, but not dangerous, and that its therapeutic effectiveness is, at the highest estimate, of a minor grade, particularly in the control of asthma, and definitely inferior to that obtainable by the parenteral injection of pollen extract.

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EFFECT OF HISTAMINASE

ON HISTAMINE INTOXICATION, TUBERCULO-ANAPHYLAXIS AND TUBERCULO-ALLERGY

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The problem of tuberculosis has been involved so intimately with the conceptions of tuberculo-anaphylaxis, tuberculo-allergy and specific immunity that within recent years it was brought to fundamentally close approximation to the conceptions evolved on the theoretical bases of histamine action in the body. These actions in general were reviewed elaborately by Best and McHenry in 1931,¹ when they pointed out that there appears to be a striking relation between histamine shock and anaphylactic shock as based on the observations of Dale and Laidlaw (1910-1920) and others. In 1929 Best² showed that lung and other tissues when suspended in saline solution and incubated in the presence of toluene at 37 C. cause the disappearance of naturally occurring or added histamine. The substance or system producing this disappearance is thermolabile. In 1930 Best and McHenry³ suggested the name histaminase for a histamine-inactivating substance with the characteristic of enzymes. They found the richest sources in the dog to be the kidney and intestine, less being present in the lungs. The histamine-histaminase reaction is inhibited by lack of oxygen and by small amounts of cyanide. Perfusion experiments showed that isolated kidneys inactivate histamine much more rapidly than liver, heart and hind limbs of the dog. They stated at that time:

Since it has not been established that histamine is the causative agent in any pathological condition there would be no obvious clinical application of histaminase, even if it should be established that the ability of an organism to inactivate histamine can be increased by administration of the enzyme.

Since that time, numerous attempts have been made to establish the identity of histamine action and disease, to apply histaminase in vivo for treatment of certain diseases and to inactivate histamine itself. A successful attempt to neutralize the toxic action of histamine by histaminase and also to prevent anaphylactic shock by the prior administration of histaminase in the guinea pig was recorded in 1939 by Karady and Browne.⁴ They found that the intravenous injection of 3 units (3 ampules) of histaminase-Winthrop (Torantil T 360) in guinea pigs—1 unit of histaminase is the amount necessary to detoxify in vitro 1 mg. of "histamine dihydrochloride"—fifteen minutes before the intra-abdominal injection of 4 mg. of histamine prevented the symptoms of histamine shock in most instances. Of ten control animals, all showed marked symptoms within five to seven minutes, and seven animals died shortly. Of the twenty animals pretreated with histaminase, six showed slight symptoms after fifteen minutes, but they disappeared in a few minutes in all but two animals, which died thirty-five minutes after the injection of the his-

tamine. Histaminase (3 units) given intravenously fifteen minutes before the intra-abdominal administration of egg white (2 cc. of 50 per cent solution) to previously sensitized guinea pigs prevented an anaphylactic shock completely in fifteen of twenty animals. The other five guinea pigs showed only very slight symptoms beginning twenty minutes after the injection of egg white and lasting for a few minutes. Of the ten control animals, all showed severe anaphylactic shock developing within five to ten minutes, and four animals died from ten to fourteen minutes after the injection of the egg white.

In the light of our recent analysis of the tubercle bacillus and its natural products by immune, allergic and anaphylactic tests,⁵ these results with histamine and

TABLE 1.—The Effect of Histaminase on Tuberculo-Anaphylaxis in Guinea Pigs

Sensitizing Infection, Amount of Tuberculoprotein in Seltz Filtrate *	Histaminase, Amount Given Intravenously (Via Ear Vein)	Amount of Natural Seltz Filtrate Given Intravenously After Sensitizing Injection	Interval Following Histaminase Injection When Intoxicated by Injection Was Given	Results
5.0 mg.	4 units	2 cc. (1.1 mg. tuberculoprotein) 60 days	15 minutes	Died 3 minutes
5.0 mg.	0 units	2 cc. (1.1 mg. tuberculoprotein) 60 days	30 minutes	Died 3 minutes
5.0 mg.	0 units	3 cc. (1.7 mg. tuberculoprotein) 60 days	4 hours	Died 3 minutes
5.0 mg.	0 units	2 cc. (1.1 mg. tuberculoprotein) 60 days	21 hours	± reaction; recovered †
5.1 mg.	0 units	2 cc. (1.0 mg. tuberculoprotein) 55 days	21 hours	Died 2 minutes
5.1 mg.	0 units	2 cc. (1.0 mg. tuberculoprotein) 55 days	21 hours	Died 2 minutes
5.2 mg.	0 units	2 cc. (1.0 mg. tuberculoprotein) 40 days	21 hours	Died 2 minutes
5.1 mg.	28 units	1.5 cc. (1.4 mg. tuberculoprotein) 72 days	30 minutes	Died 2 minutes
12.8 mg.	20 units	2 cc. (1.0 mg. tuberculoprotein) 63 days	21 hours	Died 2 minutes
12.8 mg.	20 units	2 cc. (1.0 mg. tuberculoprotein) 63 days	48 hours	Died 2 minutes

* Determined by trichloroacetic acid precipitation (Solbert). References: Corper, H. J., and Cohn, Maurice L.: The Effects of Tuberculoprotein: A Quantitative Study, J. A. M. A. 112:403-408 (Feb. 4) 1939; Intoxication in Tuberculosis, Ann. Rev. Tuberc. 11:171-80 (Jan.) 1910.
† Almost lethal.

histaminase, and anaphylaxis and histaminase, appeared to offer exceptional opportunities for the solution of a little understood problem in tuberculosis and in allergy in particular. These observations showed that the bacillary body of the tubercle bacillus sensitizes primarily to tuberculo-allergy and serves to immunize against virulent infection, while the natural filtrate containing tuberculoprotein sensitizes to anaphylaxis, provokes anaphylactic shock and allergic intoxication but does not sensitize to allergy or immunize specifically against virulent infection. From these observations, it was concluded that tuberculo-anaphylaxis, tuberculo-allergy and tuberculo-immunity show distinctive characteristics indicating that they are separate and apparently unrelated biologic phenomena.

5. Corper, H. J.: Analysis of the Tubercle Bacillus and Its Natural Products by Immune, Allergic and Anaphylactic Tests, J. Infect. Dis. 60:23-29 (Jan.-Feb.) 1940.

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By means of the appropriate use of histaminase, and in the light of Karady and Browne's observations, it was hoped that we might be able to discern whether the intoxication in tuberculo-anaphylaxis or in tuberculo-allergy, or both, was histamine shock or intoxication, whether one or both could be combated by the appropriate use of histaminase, and, if they did not react alike, possibly to obtain additional evidence of the difference in these reactions. Accordingly, the effect of histaminase on tuberculo-anaphylaxis and tuberculo-allergy in the guinea pig was studied.

THE EFFECT OF HISTAMINASE ON TUBERCULO-ANAPHYLAXIS AND TUBERCULO-ALLERGY

Accepting the previous *in vivo* observations concerning the effect of histaminase on histamine intoxication and anaphylactic shock in the guinea pig on face value, it appeared necessary in the early part of our studies to be certain of the potency of the histaminase preparations we used.⁶ Accordingly, we followed the O. W. Barlow method for *in vitro* estimation of histaminase, which had to be modified slightly for our special purposes of using a lethal test instead of the usual test involving lowering of blood pressure.

METHOD OF ASSAY OF HISTAMINASE

Buffer solution (*p*_H 7.35 to 7.4) was prepared by dissolving 7.6 Gm. of disodium phosphate (Na₂HPO₄ · 12H₂O) and 0.7 Gm. of sodium biphosphate (NaH₂PO₄ · H₂O) in 262 cc. of recently boiled distilled water. The test was set up as follows: Tube 1 contained 15 cc. of buffer solution, 3 cc. of distilled water and 1 mg. of histamine hydrochloride; tube 2, 15 cc. of buffer solution, 2 cc. of distilled water, 1 cc. (1 unit) of histaminase and 1 mg. of histamine hydrochloride; tube 3, 15 cc. of buffer solution, 2 cc. (2 units) of histaminase and 1 mg. of histamine hydrochloride. The tubes were saturated with oxygen, placed in a shaking machine for twenty-four hours at 37.5 C. and then used for intravenous (ear vein) injection in guinea pigs (no anesthetic or drugs were used which might confuse the results).

RESULTS WITH FIRST SUPPLY OF HISTAMINASE

Tube 1, Control.—Histamine hydrochloride, 3 cc. (0.17 mg.), injected into an 820 Gm. guinea pig made the animal extremely ill but the animal recovered; 5 cc. (0.28 mg.) injected into a 1,040 Gm. guinea pig was lethal in three minutes.

Tube 2.—One unit of histaminase and 1 mg. of histamine hydrochloride, 4.5 cc. (0.25 mg.), injected into a 395 Gm. guinea pig was lethal in one minute, and 9 cc. (0.5 mg.) injected into a 1,204 Gm. guinea pig was lethal in two minutes.

Tube 3.—Two units of histaminase and 1 mg. of histamine hydrochloride were used. The entire tube of 18 cc. was injected into a guinea pig without effect.

Conclusion.—Two units of histaminase completely destroyed 1 mg. of histamine hydrochloride, while 1 unit did not completely destroy 1 mg. of histamine hydrochloride.

RESULTS WITH SECOND SUPPLY OF HISTAMINASE

Histamine hydrochloride, 3 cc. (0.17 mg.), was lethal to a 1,000 Gm. guinea pig in two minutes. One unit of histaminase plus 1 mg. of histamine hydrochloride, 18

cc., was lethal to a 1,110 Gm. guinea pig in two minutes, while 9 cc. was not lethal but gave a pronounced histamine reaction. One unit of histaminase plus 0.5 mg. of histamine hydrochloride and 2 units of histaminase plus

TABLE 2.—The Effect of Histaminase on General Tuberculo-Allergic Intoxication

Sensitizing Injection Given Subcutaneously (Tubercle Bacilli)	Amount of Histaminase Given Intravenously (Ear Vein)	Interval After Sensitization and Route of Intoxicating Injection of 5 Cc. Natural Seitz Filtrate (4.7 Mg. Tuberculo-protein)	Interval After Histaminase Injection When Intoxicating Injection Was Given	Results
1 mg. avirulent human tubercle bacilli	4 units	Intraperitoneally, 101 days	15 minutes	Died 36 hours
		Intraperitoneally, 101 days	15 minutes	Died 18 hours
		Intraperitoneally, 101 days	Died 36 hours
		Intraperitoneally, 101 days	Marked toxicity; recovered
	4 units	Intraperitoneally, 40 days	15 minutes	Marked toxicity, recovered
		Intraperitoneally, 40 days	15 minutes	Died 36 hours
		Intraperitoneally, 40 days	Died 36 hours
		Intraperitoneally, 40 days	Died 22 hours
	4 units	Intraperitoneally, 40 days	24 hours	Died 15 hours
		Intraperitoneally, 40 days	24 hours	Marked toxicity, recovered
		Intraperitoneally, 40 days	24 hours	Marked toxicity, recovered
		Intraperitoneally, 40 days	Died 36 hours
0.0001 mg. virulent human tubercle bacilli	4 units	Intraperitoneally, 40 days	15 minutes	Marked toxicity, recovered
		Intraperitoneally, 40 days	Died 36 hours
		Intraperitoneally, 40 days	Died 36 hours
		Intraperitoneally, 40 days	Died 36 hours
	4 units	Intraperitoneally, 40 days	15 minutes	Died 15 hours; tuberculosis 2+*
		Intraperitoneally, 40 days	15 minutes	Died 24 hours; tuberculosis 2+
		Intraperitoneally, 40 days	Died 15 hours; tuberculosis 2+
		Intraperitoneally, 40 days	Died 18 hours; tuberculosis 2+
	10 units	Subcutaneously, 46 days	24 hours	Marked toxicity; recovered
		Subcutaneously, 46 days	24 hours	Died 18 hours
		Subcutaneously, 46 days	24 hours	Died 30 hours
		Subcutaneously, 46 days	Marked intoxication; recovered
0.0001 mg. virulent human bacilli	20 units	Subcutaneously, 46 days	Died 72 hours
		Subcutaneously, 46 days	Died 18 hours
		Subcutaneously, 81 days	24 hours	Died 21 hours
		Subcutaneously, 81 days	Died 16 hours
	20 units	Subcutaneously, 67 days	24 hours	Died 8 hours
		Subcutaneously, 67 days	tuberculosis 3+
		Subcutaneously, 67 days	Died 8 hours
		Subcutaneously, 67 days	tuberculosis 3+

* The amount of tuberculous involvement found in these guinea pigs is graded from 0 to 4+, from no visible macroscopic tuberculosis to a profound generalized tuberculosis.

1 mg. of histamine hydrochloride showed complete destruction of the histamine.

Conclusion.—Two units of histaminase completely destroyed 1 mg. of histamine hydrochloride *in vitro* as determined by intravenous toxicity in the guinea pig.

6. The histaminase was supplied for these studies in 2 unit ampules by the Wintthrop Chemical Company, Inc., which assisted during these investigations. Their original assay, 2 units per ampule of histaminase, was reassayed by them, giving 1.4 units and 1.24 units for the first and second batches respectively. This product does not stand accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

TUBERCULO-ANAPHYLAXIS

Tuberculo-anaphylaxis results in guinea pigs from the sensitization with suitable amounts of tuberculoprotein, contained in the filtrate from growing tubercle bacilli on the Wong-Weinzirl nonprotein medium, and from giving an intravenous intoxicating injection of the same filtrate containing tuberculoprotein after from two weeks to at least six months or more. The route of intoxicating injection must be intravenous in distinction to the allergic intoxication, to be considered later, in which any parenteral route can be used.

In table 1 are recorded the results of an attempt to protect guinea pigs against lethal tuberculoprotein anaphylactic shock.

In spite of the fact that the guinea pigs recorded in table 1 were given from 4 to 28 units of histaminase intravenously and that intervals varying from fifteen minutes to forty-eight hours were allowed to elapse before the intoxicating intravenous injection of tuberculoprotein (filtrate) was administered, no appreciable

TABLE 3.—The Effect of Histaminase on Tuberculin Cutaneous Reaction (Tuberculoprotein Cutaneous Hypersensitiveness)

Subcutaneous Sensitization Injection of Tubercle Bacilli	Tuberculin Cutaneous Reaction 21 Hours After Intravenous Injection of 1:100 Seltz (Tuberculoprotein) and Interval After Sensitization Injection	Amount of Histaminase Given 15 Minutes Prior to Cutaneous Filtrate (Tuberculoprotein) Injection	Tuberculin Cutaneous Reaction 21 Hours After Intravenous Injection of Seltz Filtrate (Tuberculoprotein)
1 mg. avirulent human	3+* 82 days	4 units	2+
	3+ 82 days	4 units	2+
	2+ 82 days	4 units	2+
	3+ 82 days	4 units	2+
	2+ 82 days	2+
	3+ 82 days	2+
	3+ 82 days	3+
	2+ 82 days	2+
	83 days	20 units	2+
	83 days	2+
0.0001 mg. virulent human	... 67 days	20 units	3+
	... 67 days	2+

* The cutaneous tuberculin reactions are graded arbitrarily from 0 to 4+; from no visible reaction beyond that produced by a saline control to a marked erythematous, edematous reaction about 2 cm. in diameter with a central area of necrosis.

effect on the lethal anaphylactic shock was noted. The lethal effect was not retarded in any way in comparison with the effect on guinea pigs not treated with histaminase (not tabulated here because of its similarity to the former and to conserve space).

TUBERCULO-ALLERGY

General Allergic Intoxication.—Tuberculo-allergy was produced in guinea pigs by the injection of human tubercle bacilli (avirulent or virulent). If intoxication is desired after an appropriate interval, the parenteral (intravenous, subcutaneous or intraperitoneal) injection of tuberculoprotein (filtrate) in suitable amount is administered. A profound, slowly evolving intoxication results from the second intoxicating injection, not resembling anaphylactic intoxication, with death, when it occurs, ensuing in from a few hours to seventy-two hours.

An attempt to neutralize the general allergic intoxication in guinea pigs by histaminase injected intravenously is recorded in table 2.

An examination of the data recorded in table 2 indicates that no appreciable retardation of general tuberculo-allergic intoxication is produced by histami-

nase in amounts ranging from 4 to 20 units given to guinea pigs intravenously fifteen minutes and twenty-four hours prior to an intraperitoneal or subcutaneous intoxicating injection of tuberculofiltrate (tuberculo-protein), regardless of whether the tuberculo-allergy was induced by avirulent or virulent (progressive tuberculosis-inducing) human tubercle bacilli.

Tuberculo-cutaneous Hypersensitiveness (Cutaneous Tuberculin Reaction).—Even though no effect of histaminase was noted on the general tuberculo-allergic

TABLE 4.—The Effect of Histaminase on Histamine Intoxication

Weight of Guinea Pigs in Grams	Amount of Histaminase Given Intravenously	Amount and Route of Histamine Hydrochloride Injection	Time Interval After Histaminase when Histamine Hydrochloride Was Injected	Results
1,015	4 units	0.5 mg. intravenously	15 minutes	Died 4 minutes
955	0.5 mg. intravenously	Died 2 minutes
945	4 units	4.0 mg. intraperitoneally	15 minutes	Died 45 minutes
900	4.0 mg. intraperitoneally	Markedly toxic; recovered
1,755	10 units	0.3 mg. intravenously	15 minutes	Died 2 minutes
810	10 units	0.25 mg. intravenously	15 minutes	Died 3 minutes
1,385	0.25 mg. intravenously	Died 1 minute
1,000	0.3 mg. intravenously	Died 2 minutes
1,020	20 units	0.3 mg. intravenously	15 minutes	Died 1 minute
748	10 units	0.25 mg. intravenously	30 minutes	Died 3 minutes
1,703	20 units	4.0 mg. intraperitoneally	15 minutes	Died 33 minutes
905	20 units	4.0 mg. intraperitoneally	15 minutes	Died 90 minutes
1,010	20 units	4.0 mg. intraperitoneally	15 minutes	Died 30 minutes
1,140	4.0 mg. intraperitoneally	Markedly toxic; recovered
1,240	4.0 mg. intraperitoneally	Markedly toxic; recovered
1,050	4.0 mg. intraperitoneally	Markedly toxic; recovered
226	4 units	4.0 mg. intraperitoneally	15 minutes	Died 8 minutes
255	4 units	4.0 mg. intraperitoneally	15 minutes	Died 9 minutes
203	4.0 mg. intraperitoneally	Died 13 minutes
225	4.0 mg. intraperitoneally	Died 14 minutes
846	10 units	6.0 mg. intraperitoneally	30 minutes	Died 18 minutes
872	10 units	6.0 mg. intraperitoneally	30 minutes	Died 20 minutes
818	10 units	6.0 mg. intraperitoneally	24 hours	Died 24 minutes

intoxication, it was thought possible that some effect of the histaminase might be exerted on the cutaneous hypersensitiveness to tuberculoprotein. In order to determine this possible effect, guinea pigs were sensitized allergically by appropriate bacillary injections and then were tested at a suitable time for tuberculoprotein (filtrate) cutaneous reactivity before and after histaminase treatment. The results of these tests are recorded in table 3.

The data concerning the effect of intravenous histaminase injections on cutaneous hypersensitiveness in tuberculo-allergic guinea pigs recorded in table 3 indicate that the histaminase given intravenously in amounts of 4 and 20 units fifteen minutes before the intra-

cutaneous injection of a tuberculin testing dose (1:100 dilution of natural filtrate) revealed no appreciable inhibitory effect on the development of the specific cutaneous reaction resulting in twenty-four hours, as recorded in table 3, or at any time during the usual forty-eight hours' observation period. The slight retardation in the reactions noted in the second as compared with the first intracutaneous test with tuberculo-protein, which was found both in the controls and in the histaminase-treated animals, possibly may be accounted for by a slight desensitizing effect of the first tuberculo-protein injection itself.

EFFECT OF HISTAMINASE ON IN VIVO HISTAMINE INTOXICATION

In view of the foregoing negative effects of histaminase on the intoxication of tuberculo-anaphylaxis and tuberculo-allergy, it appeared advisable to check our results. If for no other reason than for academic purposes, it would be useful in trying to explain the possible absence of the relation of histamine to these intoxications. Therefore we repeated the in vivo histaminase-histamine neutralization experiments reported by others. In our experiments attempting to neutralize a lethal toxic unit of histamine, we used both intravenous and intraperitoneal intoxicating routes. The detailed results of these experiments in guinea pigs are recorded in table 4.

The tests, recorded in table 4, attempting to neutralize histamine intoxication by prior (from fifteen minutes to twenty-four hours) intravenous histaminase injections showed no appreciable detoxicating effect of the histaminase injections on approximately 1 unit, a lethal amount, of histamine hydrochloride, regardless of whether the latter was administered intravenously or intraperitoneally to the guinea pigs, and even though the histaminase in in vitro tests using 2 units was able completely to detoxicate 1 mg. of histamine hydrochloride in twenty-four hours, as tested by intravenous injection of the final material into guinea pigs. The intoxicating dose of histamine hydrochloride given by intravenous injection was about one tenth the amount given by the intraperitoneal route.

SUMMARY AND CONCLUSIONS

In an attempt to clarify the mechanism of tuberculo-anaphylactic and tuberculo-allergic intoxication, histaminase of tested in vitro strength was given intravenously to guinea pigs, which had been appropriately sensitized prior to an intoxicating injection of the specific tuberculo-protein without, however, appreciably neutralizing or retarding the tuberculo-anaphylactic or tuberculo-allergic intoxication (general or cutaneous hypersensitiveness). In controlling these observations, it was found impossible to neutralize a single lethal general intoxicating amount of histamine hydrochloride when the histaminase was given from fifteen minutes to twenty-four hours prior to the intravenous or intraperitoneal histamine injection or when the amount of histaminase used was as much as 20 units.

From these observations, it still remains impossible to suggest whether tuberculo-anaphylactic or tuberculo-allergic intoxications or reactions are based on histamine reactions or liberation, for which purpose these experimental investigations were primarily performed. For these reasons, it would not appear that histaminase has a place at present in the therapy of tuberculo-allergic conditions.

TYPHOID FEVER OCCURRING IN IMMUNIZED PERSONS

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The success of typhoid immunization in preventing the outbreak of widespread epidemics of the disease has been so complete that there has been relatively little opportunity for studying the disease in persons so immunized.¹ When the epidemic on which this report is based developed in a population 90 per cent of which had been immunized against typhoid fever, the value of a clinical and statistical study was suggested to me.² The prevailing war conditions made necessary frequent and unforeseen changes in the personnel and eventually mass evacuations from the hospital; in the resulting confusion the detailed clinical, laboratory and statistical records were lost. Nevertheless, the experiences obtained were so informative and some of the observations so striking that I felt that even a brief communication based on my personal notes and facts vividly impressed on my memory might have some value as an addition to the literature already existing on this subject.

The military hospital at Vich, Spain, an old convent, was made ready for occupancy five days before the arrival of hospital personnel. On his arrival the medical director of the hospital consulted with the city authorities and the city bacteriologist. It was found that this old convent was supplied with water from three different sources and that the water was conducted to the convent in leaden pipes, which had been so inextricably connected up to each other that it was a several days job to separate the various sources of water supply. There were three sources which emptied into a large common iron reservoir that was placed in the top story under the roof of the convent. From the city bacteriologist it was learned that one of these sources of supply was fairly uncontaminated and constantly had a low bacterial count. The second source of supply was supposed to be fairly uncontaminated at high water, but during the dry season it was regularly contaminated with all kinds of impurities. The third source of supply, the convent pump, drew surface water from a well situated in the convent gardens, and this well, as all similar wells in the city of Vich, had been for centuries badly contaminated with typhoid organisms and all kinds of impurities. The two contaminated sources were disconnected and joined to one tank, the water of which was colored red with permanganate and led off into taps, each of which not only delivered this red water but was furthermore marked with a sign, "nonpotable water." It was necessary to have this additional supply as the needs of the institution greatly exceeded the available drinking water. The tank which contained water from the uncontaminated source of supply was thoroughly chlorinated and kept so, and this water was led off into taps that were marked "potable water." To

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2. Dr. Leo Eloesser, of San Francisco, suggested the study, outlining methods of procedure, and continued his interest in this study. He also supplied the information on the source of infection.

effect this change, however, took several days, and the infection probably occurred a good many days before this change could be made.

The epidemic broke out in the military hospital at Vieh in the last week of April 1938, about one month after the hospital had been established. At this time the hospital had approximately 1,700 patients and a staff of about 200. The source of the infection was one of three water supplies of the hospital which had become contaminated from the overflow of an adjacent sewage system. Admissions and discharges to and from the hospital were prohibited from the time of the discovery of the disease until two weeks after it had been brought under full control. Thus the population of the hospital was constant for a period of five weeks. Questioning of this effective revealed that about 10 per cent had never been vaccinated against typhoid fever while the remaining 90 per cent had received two or more injections of typhoid vaccine from one year to three months prior to the epidemic.

Altogether there were 147 cases of typhoid proved by Widal tests and positive cultures from the blood, urine or stools and in several cases from all three sources. However, in the month preceding and during this time practically everybody in the hospital suffered some form of gastrointestinal disturbance. This consisted of malaise, headache, backache, a feeling of fulness in the abdomen associated with diarrhea (less often constipation) and sometimes slight grades of fever. Owing to limited facilities laboratory studies could not be done but it is highly probable that many of these too were mild typhoid infections.

Of those with proved typhoid forty-nine had never been immunized against the disease, or approximately 25 per cent of the 190 unprotected patients and staff members in the hospital. The remaining ninety-eight patients had been previously immunized, thus giving an incidence of 6 per cent for the immunized effective of the hospital. The total incidence of the entire hospital was about 7.5 per cent.

CLINICAL COURSE

Only fourteen patients (14.3 per cent) in the immunized group showed the classic features and course of the disease as it appeared in the nonimmunized patients. Of the remaining, a third (about 28 per cent of the total immunized group) ran a mild and abbreviated but otherwise typical course of typhoid fever. The third and largest group (58 per cent of the immunized patients) was atypical in many respects and demonstrated few constant features but these were also most constant for the series as a whole. Dissociated pulse and temperature, i. e. relative bradycardia, was by far the most notable, being almost invariably present in all the cases, typical and atypical, of typhoid fever. In almost all cases the pulse was 80, 90 and rarely over 95, associated with temperatures as high as 104.5 F. Late in the course of the disease and associated with symptoms of toxic myocardial changes the pulse increased and was of grave prognostic import.

Splenomegaly was second only to the relative bradycardia as a constant feature. In the series of ninety-eight immunized patients, sixty showed some enlargement of the spleen. In the present series actual leukopenia was not a frequent occurrence, but white blood counts within normal limits were the rule even when there were marked elevations of temperature. Less impressive from the diagnostic point of view but

next in the order of constancy was the "characteristic" faeces as described in the textbooks. The appearance of the tongue with its thickly furred dorsum and flaming red borders and triangle at the tip was even more characteristic.

The exanthem varied remarkably. With some patients the eruption appeared in four or five days, with others only after two, three and even four weeks, and fully half the immunized patients never had an eruption at all. The extent of the eruption also showed all possible variations. In some cases it was represented by only four or five pastel rose-colored flecks 1 mm. in diameter on the back or abdomen and in others all possible forms were seen. The most extreme case in this series closely resembled a case described by Labbé. My case occurred in a Canadian 25 years of age who had been immunized three months before contracting the disease. He had been running the typical course of a very severe typhoid fever infection for three weeks. Absence of the eruption was the only atypical feature. Suddenly toward the end of the third week and within twenty-four hours there developed several crops of spots in rapid succession that soon involved the entire body including the face, ears, neck and extremities. Only the palms, soles and genitalia were spared. The rash was a dusky dark purplish red slowly fading on pressure, macular and possibly very lightly raised. The macules measured 3 to 6 mm. in diameter and frequently coalesced to form irregular patches up to 1 and 1.5 cm. in diameter. The exanthem was so atypical that it seemed that a mistake in the diagnosis had been made and that my associates and I were dealing with a case of typhus or, failing that, of typhoid complicated by measles. However, the positive typhoid cultures, the increasing sensitivity of the Widal reaction, the leukopenia and the apathetic and quiet status of the patient ruled out the former while the absence of Koplik's spots, coryza and conjunctivitis spoke against a complicating measles. The further course of this patient was uneventful; three days later the temperature started the usual fall by lysis, and two weeks after the appearance of the rash the patient was afebrile and the eruption, having changed to a brownish discoloration, gradually and completely disappeared.

The temperature curves fell into three main categories: the typical prolonged curve of pyrexia with gradual stages of rise and defervescence, secondly a similar curve but with all three stages shortened, and finally in the largest group, a curve with no constant features and quite variable in form.

LABORATORY DATA

Although the presence of a Widal reaction in patients previously immunized had little diagnostic import per se, the variation in its sensitivity during the course of the disease was a very valuable guide to a correct diagnosis. On admission to the typhoid ward all our immunized patients had positive Widal tests. Seventy-two were positive in dilutions of 1:40, twenty at dilutions of 1:160, five at dilutions of 1:320 and only one at the maximum dilution used, 1:640. All patients showed a progressive increase in agglutinins during the course of the disease so that at the time of discharge all but three showed positive reactions in the highest dilutions. On the other hand there were three patients with fever of unknown etiology under observation, all of whom had been immunized against typhoid fever. One of these had a positive agglutination reaction in a

titer of 1:80 and the other two positive reactions in dilutions of 1:320. Successive Widal tests showed no further increase in agglutinins. Ultimately the diagnosis of brucellosis was made in two cases and amebiasis in the third.

Stool cultures were positive in the majority of cases at least once during the illness, and the frequency of positive cultures in the immunized group approximated the frequency in the nonimmunized group. Blood cultures for the nonimmunized group were positive only slightly less frequently than the stool cultures, but in the immunized group they were only about half as frequent. This discrepancy between the approximately equal frequency of positive stool cultures for the two groups and the difference in the frequency of positive blood cultures was interpreted as signifying that the bacteremia in the immunized group was of shorter duration and therefore the positive stage escaped detection by the infrequent cultures made. Because of the shortage of materials and the difficulties of transportation it was impossible to do more frequent blood cultures to throw more light on this interesting question.

COMPLICATIONS

Complications were uncommon in both groups but more frequent among the immunized patients. There were four patients who suffered relapses, three from the immunized group and only one from the nonimmunized group. This last patient, a nurse, had a total of three relapses before overcoming the disease and during the second relapse suffered a fairly severe intestinal hemorrhage, the only case of this complication in the entire series. Bronchopneumonia developed in two patients, one from each group; the nonimmunized patient died, the immunized patient recovered. The remaining three complications occurred in immunized individuals. One had a laryngeal ulcer that healed spontaneously after a week. The second had fatal typhoid meningitis. The third, who eventually succumbed to an overwhelming toxemia, developed a complication not described in the literature. This patient had a shrapnel wound in the form of an avulsion of muscle tissue in the lateral aspect of the middle third of the left thigh, which left a cone-shaped defect about 6 cm. in diameter and 3 cm. in depth at the apex. Two weeks after the onset of typhoid this region and the tissue bordering it for a distance of 3.5 cm. became dry, black and gangrenous, resembling very much noma of the face. Cultures from this gangrenous material were not made.

MORTALITY

Nine of the total of 147 cases terminated in death thus giving a mortality rate of 6.1 per cent for the entire series. Of these nine deaths five occurred in the nonimmunized group, a mortality of 10.2 per cent for this group, and four among the immunized patients, a mortality of 4 per cent.

TREATMENT

With the exception of the use of prostigmine for the relief of tympanites nothing new in the treatment of the disease can be reported. Because the value of the well known principles of treatment were so impressively demonstrated by the conditions under which we had to work, it seems worth while to emphasize these once more here.

Absolute bed rest is one of the most essential requirements in the care of these patients. Occasionally some

of the patients would prevail on our inexperienced nurses to allow them to sit up in bed or squat alongside the bed to use the bedpan. Invariably this procedure was followed by a rise in temperature and complete exhaustion. Stimulants such as caffeine, epinephrine hydrochloride and camphor generally defeated their purpose because they greatly increased the restlessness of the patient, leading to exhaustion, rise in temperature and delirium, so that we came to prohibit these drugs unless they were absolutely indicated. Sedatives were used freely, the most effective being the barbiturates and chloral hydrate. To very restless and delirious patients who could not be controlled by these, one sixth grain (0.01 Gm.) of morphine, repeated in an hour if necessary, was given. It was gratifying to note the lowered temperature and improved appearance of the patient after a few hours of rest induced in this manner.

The problem of adequate nutrition was most difficult to solve. Butter, cream and eggs were not available. The milk was diluted and to be had only in small quantities. The bread was extremely coarse. The first two weeks of the epidemic the typhoid ward was a dismal place with bed after bed occupied by wasted patients completely apathetic and disinterested in themselves and in what was taking place about them. In desperation, caution was thrown to the winds. Protein requirements were made up by meats—canned chicken, tinned ham and bully beef—shredded and served in small portions. Caloric requirements were satisfied by puréed chick-peas, rice, toast and sugar up to the tolerance of the individual. In spite of this character of the diet, which would seem traumatic to normal intestinal tracts, striking improvement occurred in almost all patients, remarked on even by the nonmedical personnel. The patients gained in weight and concomitantly became much brighter and more interested, while the number of stuporous and delirious patients decreased notably.

The distressing and dangerous nature of tympanites in typhoid fever is usually understated. Probably because of the high sugar content of the diet and the toxicity of the particular epidemic there was a marked tendency toward distention in this series. Invariably associated with distention and roughly varying with its degree there also occurred a rise in temperature and pulse. With greater degrees of distention there occurred embarrassment of respiration, which in one case with most marked tympanites led to distinct cyanosis. Furthermore, although not occurring in any of the series presented, there is the increased danger of perforation as a result of the thinning out of the wall of the distended intestine and the ischemia resulting from the compression of intramural vessels supplying the necrotic Peyer's patches. Because the distention in this disease is of the paralytic or adynamic type, the first indication of this unpleasant complication is the decrease in peristaltic sounds. It became the practice in making rounds on the typhoid service not only to examine and palpate the abdomen but to listen to the peristaltic sounds as well.

Distention was treated by the usual measures including the reduction of the sugar content of the diet, enemas and return flow enemas. In spite of this, in three patients the distention increased to marked tympanites, one of the patients becoming cyanotic. It was then decided to try prostigmine to relieve the condition. Because of the theoretical possibility of precipitating a perforation it was used cautiously at first. It was found

that half an ampule (0.25 mg.) of prostigmine injected subcutaneously stimulated smooth mild peristalsis that caused a steady expulsion of flatus and rapid decrease in the distention. Thereafter one half ampule of prostigmine followed if necessary by the second half an hour later was given in all cases of distention that failed to respond promptly to change in diet and an enema. The drug was so given on thirty-one occasions to nineteen patients with no ill effects noted. Relief of the distention brought about striking improvement in the patient as evidenced by the clearing of the sensorium, fall in temperature and general improved comfort. With signs of impending perforation such as localized tenderness or rigidity it may be advisable to begin with very small doses or withhold the drug entirely.

SUMMARY

A series of 147 cases of typhoid fever was studied. Of the patients, forty-nine had never been immunized against the disease and the remaining ninety-eight had received two or more immunizing injections from one year to three months before contracting the disease.

The incidence was 25 per cent for nonimmunized persons and 6 per cent for the immunized. The mortality for the nonimmunized group was 10.2 per cent and for the immunized group 4 per cent.

Only 14.3 per cent of the immunized patients showed a typical typhoid course. Of the remainder, one third had an abbreviated more or less typical course while the others had a course atypical in several respects.

Constant features in order of frequency were bradycardia, splenomegaly and leukopenia.

4641 South Ashland Avenue.

Clinical Notes, Suggestions and New Instruments

SOLITARY PLASMA CELL MYELOMA OF BONE AS AN INITIAL STAGE OF MULTIPLE MYELOMA

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This communication is a case report of a 41 year old man with a lesion of the trochanteric region of the right femur. It is of interest from the standpoint of diagnosis and prognosis.

Before operation the lesion of the proximal end of the right femur was felt to be a hemorrhagic bone cyst, although the possibilities of a benign or malignant bone tumor were also considered. The pathologic report on the tissue removed at operation was plasma cell myeloma of the trochanteric region of the right femur. Operation consisted of curettage and packing of the cavity with multiple small bone chips removed from the left tibia. Following operation, therapy of 1,500 roentgens was applied to the involved area. Symptoms had begun one year prior to operation. After operation and irradiation the femoral lesion appeared to remain inactive and showed x-ray evidence of progressive repair at the operative site. The patient's general condition remained good and he resumed his normal activities.

However, when he was examined four years after operation, multiple bone lesions characteristic of multiple myeloma were found.

REPORT OF CASE

L. J., a man aged 41, married, fell down a short flight of steps in November 1934, striking his right hip. Several days later he fell to the floor and again struck his right hip. After these falls he first noticed aching and pain about the upper part of the right thigh which radiated down the anterior aspect as far as the knee. The pain gradually became more severe, and on Oct. 15, 1935, eleven months after the onset of symp-

toms, he presented himself for examination at the New York Orthopaedic Dispensary and Hospital. His past history was essentially irrelevant, his general health having always been good. The familial history was noncontributory. Physical examination on October 26 revealed that the patient was thin and fairly well developed. He held his right lower extremity protectively. The head, neck, thorax, abdomen, upper extremities and left lower extremity were not abnormal. The blood pressure was 164 systolic, 108 diastolic, while the heart was normal clinically and no signs of decompensation were present. X-ray study of the chest revealed a sclerosed infiltration in the left infraclavicular region residual from previous pulmonary tuberculosis. The lungs were normal to percussion and auscultation. The examination of interest was confined to the right lower extremity. The legs were of equal length, but there was 1 inch atrophy of the right thigh and one fourth inch atrophy of the right calf. The right hip presented a 15 degree limitation of external rotation and a 5 degree limitation of internal rotation, as well as a moderate degree of pain and muscle spasm at the extremes of all motions. There was no swelling, tenderness or palpable deformity of the right hip or thigh.

Roentgenograms of the right femur taken on October 15 revealed an extensive lack of bone structure, in a polylocular arrangement, of the greater trochanteric area and the adjacent femoral neck and shaft. The hip joint was not involved. The lesser trochanter appeared to be separated, with a soft tissue mass beneath it. Urinalysis showed an acid reaction with a specific gravity of 1.012. A trace of albumin was present, and the urinary sediment contained amorphous urates, a few white blood cells and a few hyaline casts and cylindroids. The Bence Jones urinary protein reaction was negative prior to operation. Blood studies showed 5,250,000 red blood cells per cubic millimeter with a hemoglobin of 80 per cent. The white blood cell count was 12,300 per cubic millimeter with 71 per cent polymorphonuclear leukocytes and 29 per cent lymphocytes. The blood Kline test was negative. The erythrocyte sedimentation rate was 21 mm. at the end of one hour. The blood serum calcium level was 8.4 mg. per hundred cubic centimeters. The blood serum phosphorus was 3.2 mg. per hundred cubic centimeters, and the blood serum phosphatase was 1.4 Bodansky units per hundred cubic centimeters. The blood urea nitrogen was 15 mg. per hundred cubic centimeters, and the blood uric acid was 4.4 mg. per hundred cubic centimeters. The clinical and roentgenologic diagnosis, prior to operation, was hemorrhagic bone cyst of the proximal portion of the right femur, although the possibilities of a benign or malignant bone tumor were also entertained.

On November 1 operation was performed under nitrous oxide and ether anesthesia by Dr. James W. Toumey. A 13 cm. longitudinal incision over the lateral aspect of the proximal portion of the right thigh enabled a muscle splitting approach for a subperiosteal exposure of the greater trochanter and the upper femoral shaft. An aperture 5 by 2 cm. was made through the cortex at the base of the greater trochanter, and the cyst was entered. Large connecting cystic cavities were present in the femoral neck, greater trochanter and upper femoral shaft. These cavities were partially separated by thin bony partitions. From the base of the greater trochanter the cavity extended 10 cm. up into the femoral neck and a similar distance down the shaft. The bone surrounding parts of the cysts was paper thin, especially at the junction of the neck and shaft anteriorly and posteriorly. Posteriorly there was an area 1 by 2 cm. which was devoid of bony cortex. Bleeding was severe. The cavity was filled with soft, semiliquid friable red tissue. The cortex laterally where the cyst was opened was one sixteenth inch in thickness. A frozen section of the tissue within the cavity revealed plasma cells packed together and replacing normal bone and marrow spaces. Multiple bone chips, removed with a gouge from the left tibia, were packed into the cavity after it had been thoroughly curetted of its contents. The wound was closed in layers. Because of the loss of blood at operation, a transfusion of 600 cc. of whole blood was given several hours

later. After operation the patient made an uneventful recovery. On the fourth postoperative day a long single plaster hip spica was applied to the right leg under ethylene anesthesia. Roentgenograms taken five days after operation showed the involved area to be well filled with bone chips except for the portion of the lesion lifting up the lesser trochanter, which had apparently not been reached at operation.

The material sent to the pathologic laboratory was reported as consisting grossly of numerous pieces of dark reddish soft friable tissue. On section, some pieces appeared to be old blood clot while others showed a firmer grayish homogeneous tissue interlacing as strands through the soft reddish material. There were several pieces of smooth thin cortical bone, to some of which were attached pieces of the soft tissue. Microscopically the firmer grayish soft tissue was seen to be very cellular and to have relatively little fibrous stroma. The cells, for the most part, resembled large plasma cells with prominent oval or round nuclei eccentrically placed and a considerable amount of cytoplasm. In places these cells occurred in sheets, and in other places they were scattered. The nuclear material showed coarse scattered particles often with a spokelike arrangement, and with the Unna stain a perinuclear clear zone was noted in some cells. A few mitoses were seen. There were many very thin walled vessels, some of which were closely surrounded by plasma cells.



Fig. 1.—Lesion of the trochanteric region of the right femur Oct. 17, 1935, before operation and roentgen therapy. Note separation of the lesser trochanter with a soft tissue mass beneath it.

Areas of hemorrhage were present. The pathologic diagnosis made by Dr. Walker E. Swift was plasma cell myeloma. The sections were reviewed by Dr. James Ewing, of Memorial Hospital, and Dr. Robert Moore, of New York Hospital, both of whom agreed with the diagnosis. The tumor was considered to be malignant, and future local recurrence or multiple bone involvement was considered likely. It was considered to be radiosensitive.

Eleven days after operation, roentgenograms were made of the remainder of the skeleton. They revealed no additional lesions. The right femoral and left tibial wounds healed by first intention. Examination for Bence Jones protein in the urine was faintly positive five days after operation. On December 14, six weeks after operation, the patient was transferred to Memorial Hospital for roentgen irradiation of the lesion. A total of 1,500 roentgens was given over the anterior, lateral and posterior trochanteric region, 500 roentgens being given over each approach on three successive days (December 16, 17 and 18). The anterior field measured 12 by 10 cm., while the lateral and posterior fields measured 18 by 10 cm. One hundred and ninety-eight kilowatts was used through a

0.5 mm. copper filter. The tube distance was 70 cm., and 30 milliamperes was used for fifteen and one half seconds of exposure on each of the three treatments.

Three and one half months after operation the patient was allowed up in a walking plaster hip spica. In another five and one half months the spica was removed and crutches alone were used. One year later a cane was his sole support, and two years and nine months after operation this was discarded. Frequent roentgenograms revealed progressive repair at the operative site, with no recurrence of activity of the lesion and with subsidence and disappearance of the soft tissue mass in the lesser trochanteric region. Slight pain and aching about the right hip gradually subsided and the patient's general physical condition remained good.

The patient was last seen and examined in the follow-up clinic on Nov. 18, 1939, four years after operation. He thought his general health was quite good and he was not losing weight. However, he appeared to be chronically ill and emaciated. He was working eight hours a day as a silk cutter and was painting his house in his spare time. He had recently taken a 5 mile walk. His only complaint was a mild aching about the right hip after prolonged walking or after lying on his right side. He did not complain of symptoms other than at the right hip. Examination revealed no limitation of motion, spasm, deformity or tenderness at the right hip. Laboratory tests revealed a 1 plus Bence Jones proteinuria. Urinalysis revealed a specific gravity of 1.006, an alkaline reaction and a trace of albumin. The urinary sediment contained a few mucous threads and epithelial cells. The blood studies revealed 5,320,000 red blood cells per cubic millimeter and 78 per cent hemoglobin (12.2 Gm.). There were 10,700 white blood cells per cubic millimeter, with 83 per cent neutrophils, 15 per cent lymphocytes and 2 per cent monocytes. Fifteen per cent of the polymorphonuclear neutrophils were nonsegmented and 68 per cent were segmented. The blood serum calcium was 10.3 mg. per hundred cubic centimeters. The blood serum phosphorus was 2.9 mg. per hundred cubic centimeters, and the blood serum phosphatase was 2.5 Bodansky units per hundred cubic centimeters. Roentgenograms were again taken of the entire skeleton on November 18. They revealed no recurrence of activity at the primary lesion in the right femur. However, destructive lesions were found in the right seventh rib, the left eighth and ninth ribs, each ilium and ischium, the right tibia, the skull and the third lumbar vertebra, which were characteristic of multiple myeloma. Two weeks later he was again seen complaining of pain over the left anterior chest region. Roentgenograms revealed a pathologic fracture through a lesion in the left eighth rib.

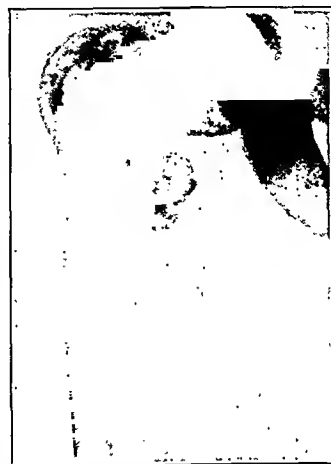


Fig. 2.—Appearance of the lesion Nov. 18, 1939, four years after operation and roentgen therapy. Slight aching was noted about the right hip, and multiple bone lesions were discovered at this time.



Fig. 3.—Chest plate showing lesions of the right seventh and left ninth ribs, Nov. 18, 1939. A pathologic fracture occurred through a lesion in the left eighth rib a few days later (not shown).

COMMENT

Some observers¹ feel that solitary myeloma of bone is a clinical and pathologic entity which is amenable to treatment and has a good prognosis. However, most authorities² believe that it is only a matter of time before a solitary myeloma of bone becomes a multiple lesion with a fatal termination. In the course of the disease such organs as the spleen, liver and kidneys may become involved.³

Cutler, Buschke and Cantril⁴ reported twelve cases of solitary myeloma of bone from the literature and five cases from the Registry of Bone Sarcoma and added one case of their own. Of the eighteen patients, five contracted multiple lesions while under observation. Of the entire group just five were living from one to ten years after operation, their lesions supposedly having remained solitary up to that time. Six of their patients presented the lesion in the trochanteric region of the femur, as does the patient here described.

It is interesting that the Bence Jones urinary protein test was negative in this case before operation, faintly positive five days after operation and definitely positive four years after operation.

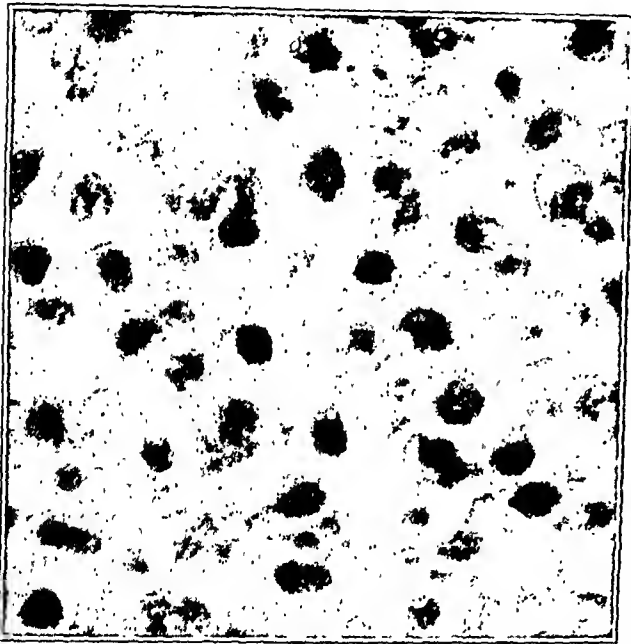


Fig. 4.—Section of tissue, $\times 800$, curetted from the trochanteric region of the right femur. Note preponderance of plasma-like cells and scanty fibrous stroma.

SUMMARY

A multiple myeloma in a man aged 41 was thought to be either a hemorrhagic bone cyst or a tumor of the trochanteric region of the right femur before operation. Roentgenograms of the entire skeleton revealed no other lesions, and tissue section revealed that it was a plasma cell myeloma. Fifteen months after operation, roentgenograms of the chest were regarded as normal. Four years after operation and five years after onset of symptoms, multiple bone lesions were discovered. Forty-nine months after operation a pathologic fracture occurred through a lesion in the left eighth rib.

420 East Fifty-Ninth Street.

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GOUT IN A SEVENTEEN YEAR OLD GIRL

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The occurrence of gout in the young and in women is uncommon; for this reason among others the following case is reported.

REPORT OF CASE:

History.—A girl aged 17 years complained chiefly of intermittent acute arthritis of the right knee of three years' duration. The family history contained one interesting feature: her mother, at the age of 20, had a uric acid stone removed from the pelvis of one kidney. She has been well since that time and has had no joint symptoms. (Her blood uric acid at present is 4.1 mg.)

The onset of the present illness was in the summer of 1931. After an 18 mile ride on a bicycle the patient began to have acute pain and swelling in the right knee. Redness was only moderate but tenderness was of extreme degree. The swelling was around the knee cap and on the sides of the knee a little below the joint. The condition was diagnosed housemaids' knee and was relieved by two weeks of rest and the use of local heat. There was no evidence of associated focal infection.

One month later the pain and swelling returned to the right knee without apparent cause. The joint disorder was considered infectious arthritis and after rest and physical therapy were instituted relief was complete.

After a few months the right knee again became swollen and very tender. On this occasion the patient was examined thoroughly and a tentative diagnosis of rheumatic fever was made. The patient was in bed one month and during the following month, after being allowed to resume activity gradually, became symptom free.

About three months later the right knee was again acutely inflamed. X-ray study revealed no abnormalities in the joint. In an attempt to eliminate foci of infection, some tonsillar remnants and adenoid tissue were removed. The leg was put in a cast for five weeks and after this the patient was on crutches for six weeks. At the end of this time roentgenograms showed decalcification to have taken place but there were no joint changes.

Following this long illness the patient became normally active and remembers no specific attacks, although she says that approximately twice a year the knee would become tender and swollen for a few days, and purgation and rest always gave rapid relief, until six weeks before admission, at which time she slipped and fell. The fall caused pain in the back and there was some swelling over the upper dorsal vertebrae. A couple of weeks later she was practicing acrobatic dancing when the right knee became painful and swollen. Laxatives were used but there was no relief, and the knee became so painful that she went to bed.

Examination.—The patient was a rather large but well proportioned and healthy looking girl. Her temperature was normal. On physical examination there were no abnormalities except those of the right knee. This knee showed a moderate amount of redness of the skin and there was slight periarticular swelling just below the knee. There was exquisite tenderness over this area. There was no limitation of motion. X-ray examination of the teeth and sinuses showed no abnormality. The white cells in the blood were not increased. The sedimentation rate of the blood was within normal limits. The uric acid content of the whole blood was 5 mg. per hundred cubic centimeters (Folin's method). Three days later it was 7 mg. and seven days later 7.5 mg. In view of the history of an intermittent "arthritis," apparently of a noninfectious type, the uric acid content of the blood and the history of a uric acid stone in the mother, a diagnosis of presumptive gout was made.

Course.—The patient was instructed to follow a diet of low purine content, and treatment was started with tincture of colchicum seed 25 drops for ten doses; this produced no diarrhea and no relief of symptoms. The blood uric acid was 7.5 mg. after the last dose. Cinchophen was then given in a dose of 0.5 Gm. six times a day for two days. On this medication the condition began to improve rapidly; the level of uric acid in the blood dropped to 5.1 mg. One week later the course of

cinchophen was repeated and following this the blood uric acid was reduced to 3.1 mg. No further medication was given and a week later the uric acid was 3.4 mg. The patient was allowed normal activity including swimming, tennis and horse-back riding, and she remained symptom free. Two months later the blood uric acid was found to be 2.8 mg., four months later 2.8 mg., six months later 3.6 mg., and now, ten months later, the patient is without symptoms and, according to her statement, in better health than she can recall in the past three years. She is still following a low purine diet and has had no further medication.

COMMENT

The emotional outlook of this girl has been changed by the diagnosis of gout and the relief of her symptoms. She had learned to dread the frequently recurring arthritis and had begun to fear a life of chronic arthritis with invalidism. Now, even though she may have a recurrence of joint pain, she will understand to some extent how to control it.

The occurrence of gout in a young girl is unusual because 98 per cent of cases of gout occur in males (Hench) and the peak in age incidence of the disease is from 40 to 50 years.

The frequency with which gout has been diagnosed in the past few years has varied in different clinics. As Hench¹ has suggested, this is due in part to the attitude of the physician, whether "conservative" or "liberal." If too conservative, early gout will not be recognized because tophi, the pathognomonic signs, are not usually present until late in the disease. The more liberal view admits that gout can be diagnosed with considerable certainty in the early stages when tophi are absent. The term "presumptive or pretophaceous gout" may be applied to such cases, following the suggestion of the American Rheumatism Association.² Accordingly, all gout diagnosed early must be "presumptive." Hench believes that probably 50 per cent should belong to this group. Jacobson,³ in a study of blood uric acid, classified twelve of his twenty-one cases as "presumptive."

The diagnosis of presumptive gout can be made fairly accurately by a careful history and by studies of the uric acid content of the blood. The history is that of a recurring acute "arthritis"; during the first few years there are no symptoms between attacks and no residual joint changes. These attacks may or may not be related to excessive indulgence in food or alcohol; they are often related to trauma. There may or may not be a family history of gout. The uric acid content of the blood is usually but not always elevated in untreated cases regardless of the stage of the disease. Jacobson found the serum uric acid level in twenty-one cases of gout to be over 7 mg. per hundred cubic centimeters of blood in nineteen cases and over 6 mg. in twenty cases. Some authors have reported a lower level of uric acid in the blood in cases of true gout. Thus Monroe⁴ recorded cases in which the uric acid content of whole blood was between 4.4 mg. and 6.5 mg. On the other hand an elevated uric acid content of the blood does not always mean gout, and a history of recurring acute arthritis must be present for a positive diagnosis to be made. Since the symptoms are not continuous from the onset, a chronic nonremitting arthritis with an elevated uric acid in the blood is not due to gout. To recognize gout more often one must be "gout conscious" and obtain a careful history of the attacks; to be conservative and not diagnose gout too often one must also be guided by definite criteria, which include the history, increased uric acid in the blood and, in true (later) gout, tophi.

SUMMARY

A girl aged 17 years with presumptive gout of three years' duration had a uric acid content of the blood during an attack varying from 5 to 7.5 mg. per hundred cubic centimeters.

Probably 50 per cent of gout must be classed as presumptive gout, which is pretophaceous and usually early gout.

Medical Arts Building.

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Special Article

CONFERENCES ON THERAPY

TREATMENT OF BLOOD DISORDERS

VI. PERNICIOUS AND OTHER MACROCYTIC ANEMIAS

NOTE.—These are the actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments and institutions. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Treatment of Blood Disorders: VII. Leukemia, Agranulocytosis and Neutropenia."

DR. MCKEEN CATTELL: Dr. West, of the College of Physicians and Surgeons, has consented to introduce the discussion on macrocytic anemias.

MACROCYTIC ANEMIAS

DR. RANDOLPH WEST: Briefly, the macrocytic anemias can be conveniently classified on the basis of Castle's experiment. First, Dr. Minot found that the feeding of one-half pound (225 Gm.) of liver daily brought about improvement in patients with pernicious anemia; secondly, Castle found that by mixing normal gastric juice with beefsteak and administering that by mouth an improvement could be obtained similar to that obtained by feeding liver. Castle therefore assumed that there was in the diet an extrinsic factor which was heat stable and in the stomach juice a thermolabile factor, which he called the intrinsic factor; that these reacted together and formed the finished material, which was then absorbed and stored in the liver and released through the circulation and brought about the maturation of the marrow red cells, which then entered the circulatory blood.

Addison's pernicious anemia is due to a lack of the intrinsic factor. Almost all persons with this disease have atrophy of the mucosa of the stomach and practically no secretion of gastric juice. Secondly, there are macrocytic anemias due to a faulty diet, as exemplified in pellagra and tropical sprue, in which the diet is particularly deficient in proteins and probably in some of the accessory food elements. Thirdly, there are cases in which both the diet and the gastric juice are adequate but in which there is an impaired absorption from the intestine. This is a large factor in tropical sprue, and as the intestinal condition improves and absorption improves the anemia also improves. Fourthly, there are certain cases of Laënnec's cirrhosis in which an anemia develops which is probably due to lack of proper storage of antianemic principle in the liver. Not all cases of cirrhosis with anemia respond to liver extracts, but a certain number do, and liver therapy is worth trying. This outline gives a working classification of the macrocytic anemias, the peripheral blood picture of which you are already familiar with. The distinguishing features are, of course, large red cells well filled with hemoglobin and a color index greater than 1.

As to the treatment of these different anemias one may consider first the liver preparations available and then the stomach material. As to liver therapy, the original Minot diet contained one-half pound of whole liver daily, and its use brought about improvement of both blood and spinal cord lesions in patients suffering from pernicious anemia. Shortly afterward many

workers began the attempt to identify the material in liver which was active in pernicious anemia. Progress has been slow, as there is no test for activity except that of improvement in patients. The active material is in all probability a peptide of a molecular weight less than 10,000 and more than 5,000, as judged both by the ultracentrifuge and by passage through graded membranes. It contains none of the known vitamins. Thiamine, riboflavin and nicotinic acid are absent. It does not appear to fit into any known part of the vitamin B complex unless possibly it acts as the protein fraction which must combine with riboflavin and some of the other vitamins in order to render them active. The yellow ferment contains protein in addition to riboflavin phosphate. But that liver material may act in this way is at present mere speculation.

As soon as injectable liver preparations were available, it was found that the materials were much more active on parenteral administration than on oral administration; and while it was necessary to eat one-half pound of liver daily to get maximal blood responses, a single parenteral injection of extract obtained from as little as 10 or 20 Gm. of liver would bring about maximal responses of the blood. Therefore it was assumed that the active principle was either destroyed in the gastrointestinal tract by the various enzymes or poorly absorbed from the intestine. The material is thus from fifty to a hundred times as effective when administered parenterally as it is when administered orally. The question as to whether one substance in liver has to do with both blood and spinal cord lesions has not been settled and cannot be settled until the material is isolated in chemical purity. The purest preparations are still mixtures and not chemical entities.

That raises a point in therapy as to whether one should treat patients who have spinal cord lesions with the highly purified concentrates or whether it is desirable to use the cruder extracts possibly containing as yet unidentified factors that may influence the cord lesions. I think that most physicians prefer the crudest injectable extract for treating spinal cord involvement. If the blood alone is involved the more highly purified forms are more convenient and less painful to the patient.

The available stomach preparation has been, as you know, ventriculin, which was developed by the Ann Arbor group. They found that desiccated unheated hog's stomach when administered by mouth brought about the same improvement that was obtained with liver. They were feeding presumably both extrinsic and intrinsic factors; the muscle and the mucosa of the stomach presumably reacted just as the beefsteak and the gastric juice had done. The results have been excellent. It is necessary to feed 10 or 20 Gm. a day to bring about improvement. Some reports have appeared in the Scandinavian literature stating that stomach preparations are superior to liver in treating the cord lesions, but I think the evidence is not convincing.

The tropical macrocytic anemias of pellagra and sprue are not simply deficiencies of antianemic material alone, as you know. In pellagra the therapeutic effects of nicotinic acid and cozymase have greatly clarified this situation. All the crude liver extracts are rich in these factors, and it was observed before the isolation of nicotinic acid that very large doses of either parenteral liver extract or oral liver extract brought about improvement in pellagra. Nicotinic acid, when admin-

istered to pellagrins, has never brought about any improvement in the blood picture, and there has been no hematologic response to nicotinic acid in the anemia of pellagra or in pernicious anemia, but the blood improves when antianemic liver material is administered. There is at least a double deficiency there of antianemic material and nicotinic acid in those pellagrins who have anemia. Possibly in some cases iron too is lacking as well as other as yet undiscovered substances.

In the individuals with tropical sprue one also gets the impression of a multiple deficiency in which both liver material and other factors, some of which are known and some of which are not, are lacking, and again the cruder extracts of liver are considered much superior to the highly purified ones in the treatment of this condition.

While a really good test for absorption of liver principles from the gastrointestinal tract in man is lacking, it can be shown that the intestinal absorption of patients with sprue is at fault by their response to the various forms of liver therapy. In the old days there were numerous diets for treating tropical sprue. The gastric juice is normal in from 70 to 80 per cent of the cases, and the feeding of a high meat diet was followed by good results in perhaps 10 per cent of the cases. Dr. Ashford always used a high beef diet and at times used liver too. The impression of the group at Puerto Rico is that on a high meat diet about 10 per cent improved. With the advent of liver therapy, perhaps 25 per cent showed marked and rapid improvement in symptoms. With the introduction of crude parenteral liver extracts injected intramuscularly, improvement is obtained in 80 per cent of the cases or better. So the parenteral route has great advantages and is much more effective than the oral route owing to abnormal intestinal physiology in persons who are suffering from tropical sprue. They also almost certainly lack iron and a number of the other vitamins as well.

As to the patients with cirrhosis of the liver, we have had only a few who have responded well. Several have had reticulocyte responses and a rise in red count and hemoglobin and also have had a sense of well-being following administration of parenteral liver extract. I do not want to become involved at the moment in the treatment of cirrhosis with high vitamin diets because that is a little aside from the subject under discussion.

Perhaps the most interesting group of patients with pernicious anemia are those with spinal cord lesions, and I should also add peripheral neuritis, because there is good evidence that persons with Addison's anemia, in addition to having the usual degeneration of the pyramidal tracts and the dorsal columns, also have a spotty peripheral neuritis, and there is some evidence accumulating that they are suffering from a vitamin B₁ deficiency in addition to their other troubles. The treatment of the cord lesions is extremely important, and it is the consensus that the results are good when one is sufficiently persistent. The administration of very large amounts of liver extract every day while the patients are in the hospital, in an attempt to saturate them with it, and then after discharge the injection of large doses once or twice a week over periods of months or even years, have I think in every instance led to an arrest of the disease or to improvement. We have two men who were paralyzed from the waist down, with the bladder and rectum out of control. One had had the

disease for only about two months, while the other had had it for a number of months; but both of them have reached the point where they get up and walk about without canes or crutches, and they have been followed for three years. The effects of sufficiently persistent treatment may be extraordinary. As some one pointed out several years ago, it is imperative to make every effort to keep the blood count of the patients at or above 5,000,000, if it is at all possible to do so. In other words, those with any sign of cord lesions should be overtreated and the blood kept absolutely normal if that can be done—and in the great majority of instances it can be done.

It is certain that the cruder extracts are effective in treating this group with neurologic lesions. It is an open question whether the most highly purified extracts are. This point is being investigated by several workers but will obviously take several years to settle.

ACTION OF LIVER

I think the last and perhaps most interesting point to be discussed is the mechanism of the action of liver material, and there are one or two discrepancies in this connection that might be worth mentioning. It is known that both pepsin and trypsin can destroy the intrinsic factor. If gastric juice is incubated at a p_H of 1 or 2, the intrinsic factor is destroyed. If the juice is neutralized as soon as it is drawn, pepsin is inactivated and the intrinsic factor can be preserved for a long period of time. If trypsin is added, the intrinsic factor is again destroyed on incubation. In experiments in which beefsteak and gastric juice are incubated together at p_H 6 or 7, which is the p_H at which the intrinsic factor acts, it has not been possible to obtain a potent injectable extract. If the intrinsic factor is fed by mouth, it works very nicely. Whether or not something additional happens in the intestinal wall or at some other point is an open question.

There is one other peculiar situation. One can feed one-half pound of kidney a day, and it works just the way liver does by mouth. If, however, one prepares an extract of kidney, as with liver, one ends with no potent material at all. Presumably the active material in kidney is combined with protein and precipitated out during the first step in the purification, which is removing protein coagulable by heat. We know that the active liver material is precipitated from aqueous solution by taurocholic acid and by nucleic acid, as well as by a number of other precipitants. It is possible that the failure of the combined intrinsic and extrinsic factors to yield an injectable potent extract is analogous to the failure to obtain potent kidney extracts.

As to the mode of action of the most highly purified active liver materials, unfortunately almost nothing is known. Dr. Rhoads has advanced evidence favoring the hypothesis that it neutralizes toxic products formed in the intestine or elsewhere in the body. Some agree with that; others do not and feel that liver material corrects a deficiency. Dr. Mosenthal years ago showed (the work was reported in the *Bulletin of the Johns Hopkins Hospital* about 1916) that if patients with pernicious anemia were fed on a diet very high in nitrogen (he did not specify the type of nitrogen in the diet so we do not know whether it included liver), as they went into positive nitrogen balance the red blood count rose. Dr. Bassett, of Rochester, has done careful balance studies on patients with celiac disease and has not been able to demonstrate any improvement in the

absorption of protein by the addition of liver extract to the diet. We simultaneously determined the nitrogen balance, plasma and red cell volume of a patient with macrocytic anemia, in order to see whether after the administration of parenteral liver extract the patient went into positive nitrogen balance before the blood improved or whether the blood improved before the patient went into positive balance. The result was very striking. The patient was in negative balance over the first ten day period and lost 11 Gm. of nitrogen over the nitrogen intake. There was no change in the total plasma nitrogen and there was an increase of about 50 Gm. in red blood cell nitrogen, which represented a mobilization of red cells from the bone marrow into the peripheral circulation. The liver extract released red cells from the bone marrow into the peripheral circulation, causing a measurable increase in blood nitrogen before the body as a whole went into positive nitrogen balance. So the effect of the liver extract is not primarily on nitrogen balance. Efforts to incubate cultures of bone marrow with active material have led to no significant changes so far. The fact remains that at the present time it is not known how the material acts and whether or not it fits into one of the enzyme systems.

DISCUSSION OF QUESTIONS

DR. PAUL REZNIKOFF: I wonder if you could tell the group in a few words how you treat a patient who has a relapse, how much liver extract you give and of what particular type, and how you vary the dose as the patient improves.

DR. WEST: When a patient is admitted to the hospital with a red count of 1,000,000 and no cord lesions and we want to start treatment immediately, we have been using injectable liver extracts and not the stomach preparations. The dose is stated in units, and 1 unit is defined as that amount of material which when administered daily will induce a satisfactory response in the reticulocytes, red cells and hemoglobin. We inject daily 1 cc. of an extract containing 15 units per cubic centimeter for the first week and then give it three times a week until the patient leaves the hospital. After that the dose is 1 or 2 cc. a week until the blood is normal, and then 1 cc. every one to two weeks, depending on the patient's needs. The blood is kept at the normal level. If the patient has spinal cord lesions we use the crudest injectable product containing 1 or 2 units in 3 cc. and give 3 cc. instead of the 1 cc. dose of the more highly purified product. Otherwise the plan is about the same. A weekly dose of from 3 to 6 cc. will usually maintain the blood level after it is normal and cause arrest or improvement in the cord symptoms. If these are very severe we use larger doses. In the older age groups one has to give more liver extract, and the needs of each patient vary greatly. One will need 3 cc. every three weeks; another will have to have 6 cc. a week.

DR. REZNIKOFF: How many units in 6 cc.?

DR. WEST: A dose of 6 cc. of the cruder extracts contains 12 units, so the dose is in the neighborhood of 12 units given in from one to three weeks' time. What dose do you use?

DR. REZNIKOFF: That is approximately what we use.

DR. HARRY GOLD: When do you use ventriculin?

DR. WEST: In the cases with bad cord symptoms, when we want to do everything possible, we use large doses of parenteral liver extract plus ventriculin by

mouth, always taken at the meal at which there is a slice of liver or meat. Castle's experiment calls for one-half pound of beefsteak plus 200 cc. of gastric juice every day. Reimann found that if one mixes 15 Gm. of liver (which produces no response when given daily by itself) with 15 cc. of gastric juice and administers the mixture every day, maximal responses are obtained. Liver is an excellent source of extrinsic factor in addition to finished material, and the stomach-liver preparations are probably the most potent of all. So we have tried to take advantage of that fact in bad situations by giving, in addition to the parenteral liver, a little rare liver plus ventriculin once a day or at any rate several times a week.

Dr. GOLD: Grain for grain, ventriculin is more potent than liver, is it not?

Dr. REZNIKOFF: Yes.

Dr. WEST: For ventriculin, 20 Gm. daily is the usual dose when the blood level is low. In favorable cases 10 Gm. of ventriculin a day is effective in maintaining the blood level once it is normal.

Dr. REZNIKOFF: Has anybody attempted to isolate the potent fraction from ventriculin?

Dr. WEST: Nobody has yet made a potent extract of ventriculin, and nothing is known of the chemical nature of the active material in it.

Dr. CLAUDE E. FORKNER: I wonder what modifications Dr. West would make in that treatment when the condition is sprue rather than pernicious anemia.

Dr. WEST: In tropical sprue we would use a crude injectable extract and try to give 8 cc. a day parenterally. In addition to that we would supply a diet which is rich in all the accessory food factors. We rely on liver and brewers' yeast for our vitamin ration, assuming that in addition to those vitamins already described there are probably several more that have not been isolated yet, and they are probably present in liver or yeast.

Dr. REZNIKOFF: How do you explain the good effects obtained in certain cases of pernicious anemia by Wintrobe and by Goldhamer, with large amounts of yeast alone?

Dr. WEST: That raises a very nice point. Wintrobe fed 120 Gm. of dried yeast a day and had excellent responses in pernicious anemia. With liver, 250 Gm. (wet weight) is fed daily. Yeast probably contains either finished material or both intrinsic and extrinsic factors.

Dr. REZNIKOFF: Goldhamer has shown that all pernicious anemia patients have some intrinsic factor and that if they are given a large amount of extrinsic factor they will, by a sort of mass action phenomenon, increase the intrinsic factor output to an effective degree. Do you think that is a tenable explanation?

Dr. WEST: Yes, that is certainly one possibility. There is another interesting observation that might serve as a point of departure for further chemical work on the active materials. Normal urine given daily as a retention enema of about an ounce or so (30 cc.) to patients with pernicious anemia produces a reticulocyte response and increase in red cells and hemoglobin. The urine of patients with pernicious anemia produces the same effect, even though the donor's blood count is low. The material in urine may be simpler to work with than that in liver. However, no chemical work has been done on it.

Dr. EUGENE F. DU BOIS: You said that in treating spinal cord patients you kept the red blood count at 5,000,000 or above. Is the red count in itself significant in helping directly the cord lesion or is it just an indication of something else?

Dr. WEST: We have assumed that it is an indication that ample antianemic material is present in the body. It has not always been possible to maintain red cell levels at 5,000,000, but we have endeavored to do that, feeling that possibly blood had first call on what material was available and the rest went to the central nervous system. Incidentally, of the purified liver materials it is certain that a single injection of 20 mg. will give a maximal response. That is down pretty close to the vitamin dose, and Strandell has reported 2 mg. a day as giving maximal responses. That has not been confirmed, and Strandell's material which appeared on the market is a peptide too.

Dr. JANET TRAVELL: Are there any toxic effects with these very large doses of liver?

Dr. WEST: On giving more than one-half pound of liver a day, the symptoms of insulin shock have been noted. There is a blood sugar lowering principle in liver which has not been identified. For the extracts given in the doses that we have mentioned, I have not seen any bad effects aside from occasional reactions, with peripheral circulatory collapse occurring unpredictably.

Dr. TRAVELL: With intravenous injection?

Dr. WEST: No, occasionally with intramuscular injection; not more than once in two years. I do not know what the explanation is. Have you had any such reactions in the New York Hospital?

Dr. REZNIKOFF: Yes, we have. On one occasion we were reasonably certain that the material entered a small blood vessel. We noticed blood at the end of the needle, although no blood appeared in the syringe before we injected the material. Another reaction we could not explain as we were reasonably certain we did not inject into a blood vessel.

Dr. TRAVELL: Do the reactions tend to appear in the same person?

Dr. REZNIKOFF: No, with the exception of two patients who have a fever and urticaria on every injection of liver of any type we have given them.

Dr. WEST: We have not seen any urticaria.

Dr. REZNIKOFF: One of our patients had a terrific reaction to purified liver extract, with a high fever and urticaria, so we never gave it to him again.

Dr. WEST: We have generally switched to ventriculin by mouth or else one of the highly purified preparations if a patient has had a reaction.

Dr. FORKNER: I think it should be mentioned that, although these preparations are labeled 15 units per cubic centimeter, the manufacturers fortify themselves with the statement that they contain an excess over that amount in order to be sure that there are at least 15 units in a cubic centimeter.

Dr. CATTELL: Is it known whether vitamin B₁₂ is a factor in the improvement of the spinal cord lesions?

Dr. WEST: It is hard to answer that. I think one can say this: that preparations of liver extract which are free of vitamin B₁₂ bring about improvement in cord lesions, but whether vitamin B₁₂ in addition would accelerate that process I don't know.

DR. CATTELL: Do you give additional thiamin chloride in such cases?

DR. WEST: We have not up to now, but we are thinking about it.

DR. REZNIKOFF: We have been doing it, and we have an impression that it helps in some cases.

DR. GOLD: Do you ever stop treating a patient with Addison's anemia?

DR. WEST: They often do that themselves for us, and the results have been variable. One man stopped treatment for a year or a year and a half and nothing happened at all. He was all right and had a normal blood count at the end of that time. Then in others, especially those on the verge of cord symptoms, marked spinal cord lesions will often rapidly develop.

DR. GOLD: Does the intermittent course of this disease still apply?

DR. WEST: One cannot tell now. The pattern of the disease in the preliver era was, as you know, first down and then in some instances up with several spontaneous periods of improvement, with an average prognosis of about three years. Even then transfusions made the basic pattern hard to follow.

DR. REZNIKOFF: Have you noticed that some of your patients respond to liver extract with a polycythemia, and some of them will run for a year or more with 6,000,000 red blood cells?

DR. WEST: Some have had counts above normal.

DR. TRAVELL: Without liver extract?

DR. REZNIKOFF: Continuing liver extract, but the blood level shoots way up, and when a student looks at the patient in the clinic he says he must have polycythemia.

DR. WEST: Yes, certainly some of them look like red Indians.

DR. FORKNER: Have you observed any spontaneous remissions in pernicious anemia that you thought were not due to treatment?

DR. WEST: Not since the introduction of liver. Before that we had several, but these patients had been given transfusions.

DR. FORKNER: In going over the data on spontaneous remissions in pernicious anemia, I think it is very questionable whether many patients have spontaneous remissions. Perhaps not more than 10 per cent do, and those remissions which have been recorded in the literature can almost always be explained on the basis of transfusions or the administration of arsenic or some other treatment.

DR. WEST: That is very interesting. I had not realized that.

DR. FORKNER: Prior to the introduction and use of arsenic in pernicious anemia, the incidence of remissions was in the neighborhood of 10 per cent or less; whereas after arsenic was used—as it was in almost every case up to 1926—the incidence of so-called spontaneous remissions jumped remarkably. That was first noted by Sir William Osler.

DR. REZNIKOFF: Do you know whether Dr. Fehr's case of the woman who ate *pâté de foies gras* every day is really authentic? It is an interesting story.

DR. WEST: I have heard the story. Her condition is supposed to have been recognized by the elder Dr. Janeway, and she outlived all her physicians. She had a passion for *pâté de foies gras*.

DR. FORKNER: I wonder if you would care to make any remarks about certain of these macrocytic anemias which are refractory to all types of treatment with liver and liver extract, those which seem at first to present a clinical picture somewhat like that of aplastic anemia.

DR. WEST: Another type that should have been mentioned is the anemia of pregnancy. The pregnancy group have been carefully studied in Boston and have been found to respond to liver or iron, or both. The great majority clear up after pregnancy. In a few classic Addison's anemia develops and in an occasional one aplastic anemia. Aplastic anemia also follows infections and exposure to various chemicals. Many of the refractory anemias have the hyperplastic bone marrow and not atrophic fatty marrow. One gets the impression that there are large numbers of red cells in the marrow, but they are unable to reach the peripheral circulation. So far there has been no response to liver, iron, copper or arsenic or sex hormones. Without any real evidence I have always thought of those conditions as being the analogue of an adenoma. The marrow is anatomically hyperplastic but functionally aplastic. An analogous process in a glandular organ would be an adenoma.

DR. REZNIKOFF: Have you had any patients who did not give a reticulocyte response but did show an increase of red cells with liver extract?

DR. WEST: I do not think we have had any.

DR. REZNIKOFF: They have been reported.

DR. WEST: They have been reported, but I have never seen one. Another puzzling problem is presented by the occasional patient with a million or so red cells who, while showing a 60 per cent reticulocyte response to a large dose of liver, still remains without change in the red cell count. Is there any explanation for that?

DR. FORKNER: Very careful studies show that the blood frequently goes up in steps. I think that often a case of pernicious anemia will seem to remain stationary at a level for perhaps a week or so and then suddenly show improvement. I don't know the explanation for that.

DR. REZNIKOFF: We have had patients who have responded to some degree, to 3,000,000 or 3,500,000 red cells, and then with massive doses of liver extract would go no further. We have then given those patients ventriculin, and I think in most cases we have observed good responses. What is the present status of the theories on the multiple chemical factors necessary to mature red cells? I am referring to Jacobson's work.

DR. WEST: The workers have modified their position and now hold that there are a primary factor, which is a peptide, and several accessory factors. Nobody has confirmed that. I think the peptide is in very good repute. Dakin first described it. An independent confirmation was made by Karrer in Switzerland, who has isolated an active mixture of peptides. For several years he thought that the phosphorus content of liver extract paralleled activity, but he got rid of the phosphorus, and the peptides were active. Strandell's material is also salted out with ammonium sulfate.

DR. TRAVELL: I should like to ask Dr. West if there are any indications for the use of iron in these macrocytic anemias.

DR. WEST: I think it has been shown that the plasma iron after the administration of liver extract actually drops during the tremendous call for iron during the synthesis of red cells; and although the body usually

has enough stored in the various organs to meet that demand, there are certainly some instances in which there is a shortage of iron in addition to liver material, and recovery will be accelerated by giving both. On the other hand, if one gives both liver and iron simultaneously, it is not possible to tell which one is effective, and the patient may continue to take liver for the rest of his life when he needs only iron. Always give one thing at a time simply from the diagnostic point of view. When the two are given together, one cannot be sure which one is effective.

DR. TRAVELL: Would you try the iron before the liver?

DR. WEST: I would decide which type of anemia the patient had and then use iron or liver first as indicated.

DR. GEORGE A. SCHUMACHER: I should like to ask a question. With malignant neoplasms anywhere in the body, except in the stomach and sometimes in the ascending colon, one frequently finds a microcytic hypochromic anemia. It is reasonable that, if there is a carcinoma in the stomach, a macrocytic anemia might develop and that would fit into your first type, but how do those anemias following neoplasms arising elsewhere fit into your classification?

DR. WEST: I simply do not know, but I think that the anemia of carcinoma of the stomach often responds to liver while the anemia of carcinoma of the ascending colon is often microcytic. Only the stomach group have been helped with liver and iron.

DR. REZNIKOFF: Only in carcinoma of the pylorus have we had fairly good results.

SUMMARY

DR. CATTELL: The therapeutic problem in the macrocytic anemias has been clarified in recent years by the recognition of the condition as a deficiency disease and the unraveling of at least some of the underlying pathologic conditions. The antianemic factor is now known to be stored in the liver. Castle's studies have shown that this substance has its source in the interaction of a heat stable substance present in meat and other protein foods (extrinsic factor) with a thermolabile material present in normal gastric juice (intrinsic factor).

Depletion of the antianemic factor occurs as the result of a number of causes, the most important being a lack of the intrinsic factor occurring in pernicious anemia, an inadequate diet giving rise to the macrocytic anemia in pellagra and tropical sprue, impaired absorption in sprue, and finally the failure to store the factor in certain cases of cirrhosis. The active material in liver has not been identified but is probably a peptide and does not correspond with any known vitamin. Various theories of its action in maintaining normal hematopoiesis have been proposed, but as yet no satisfactory proof of its role has been obtained.

The objective of treatment then is the restoration of the antianemic principle, and this is done by the administration of liver or extracts of liver. These are effective by mouth, but by this route the extracts are only from one fiftieth to one one-hundredth as potent as when given by intramuscular injection. Liver is rich in the extrinsic material as well as the finished antianemic principle and of course also certain large amounts of the various vitamins. The impression prevails that the crude extracts are more effective, especially in relation to the cord lesions, than are the more highly purified concentrates of the antianemic principle. In cases of marked involvement of the nervous system

it is recommended that liver therapy be supplemented with ventriculin, a preparation of the hog's stomach containing both the extrinsic and intrinsic factors of Castle, which is very effective in producing a reticulocyte response and in maintaining the normal blood picture.

In a fully developed case of pernicious anemia an injection of 15 units of extract is given daily for the first week and then three times a week until the patient leaves the hospital. After that a dose of from 15 to 30 units is given once or twice a week until the blood is normal. The dose may usually then be reduced, most patients requiring only 15 units every one or two weeks. With cord lesions the treatment is more vigorous and the crude preparation extracts are employed, the attempt being made to maintain the red blood cells at five million or more. This treatment may be supplemented with the oral administration of liver and ventriculin, the latter in amounts of about 20 units a day with meals.

Iron is usually not required and should be withheld at least until after the effectiveness of liver therapy has been ascertained.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

BASMETER NOT ACCEPTABLE

Manufacturer: High Tension Electric Corporation, 118 West Twenty-Second Street, New York.

Many inquiries concerning the Basmeter have been addressed to the Council. The advertising referred to the Council indicated that the medical profession was being solicited actively by the manufacturer for prospective users. That the Council might fulfil its assigned function (since the product was not submitted) it procured a Basmeter on the open market for investigation and report.

According to the advertising, "The Basmeter is a new method of calculating the Basal Metabolic Rate by means of a simple slide rule principle. It eliminates the usual objections to taking a B-M-R, such as time, space, and preparation." The clinical data required for the use of the device are blood pressure, systolic and diastolic; pulse rate; respiratory rate; age; body weight. A correlating factor, "Factor J," is determined in one of the intermediate steps. The Council examined the device and compared the basal metabolic rates determined by use of the Basmeter to results obtained using established and accepted methods.

To compare the accuracy of the device, a random sample was obtained of hospital records of patients on whom blood pressure was taken at the time of the B. M. R. determination by a fully qualified and experienced technician working under the direction of a physician. The technician made the determination on all incoming patients as a part of the physical examination. The metabolic determinations were made with an accepted instrument. Pulse rate and respiratory rate counts were for full minute periods.

These comparisons show that:

1. A most critical variation in the rates determined by the Basmeter can be produced in the results by a variation in pulse rate. This may be a change from minus 14 to plus 100 with a change in pulse rate of only one beat per minute.
2. The determination of blood pressure, which inherently is subject to a possible variation of several millimeters of mercury, can affect the calculated rate by the Basmeter in a like manner and to a similar extent.
3. The unpredictable variation of the "Factor J" with slight variations in any one of the several physical factors is apparently the main source of lack of agreement in the calculations.

The correlation between this "Factor J" under given physical conditions but varying age groups is likewise unpredictable.

A reprint sent with the device, describing the theories behind the rationale for its construction, claims close agreement between its results and hospital records—"within 1 to 1½ per cent in all but two of 1,200 cases"—yet results in the Council's survey show an agreement within 2 per cent in only ten cases of 154.

The invoice received with the device carried a typed recommendation that the user read "Standardization of Blood Pressure Readings" (THE JOURNAL, July 22, 1939, p. 294). This article not only gives definite information on methods but also states that, when careful studies of the blood pressure are to be made, the use of basal blood pressure conditions should be considered. However, although it is specified that the blood pressure should be carefully taken, in the directions for the Basmeter there is a specific claim that the Basmeter eliminates the need for omission of the morning meal and for a long period of rest.

From data compiled by the Council, it would appear that the calculation of the metabolic rate by the Basmeter gives results which are not in agreement with previously determined correlations, as will be demonstrated. Tables were compiled which were based on hypothetical but normally possible variation in single factors used by the Basmeter, the others remaining constant. These tables showed that there was an unpredictable discontinuity in basal metabolic rates, as for example:

Purely hypothetical case chosen in one of the many "critical" points on calculator: Blood pressure 170/100, age 45, weight 150 pounds, respiratory rate 22.

Pulse 74, B. M. R. — 50; pulse 75, B. M. R. + 99.

To avoid a possible criticism that the previous example is improbable, the following one is taken directly from an example in the reprint with the Basmeter:

Age 41, blood pressure 140/80, pulse rate 85, respiratory rate 16, weight 150 pounds, B. M. R. 5. Now if only the pulse is varied, the calculated results are as follows:

Pulse rate 87, B. M. R. — 37; pulse rate 84, B. M. R. — 15; pulse rate 83, B. M. R. + 35.

(Further tabular data will be included in a reprint which may be obtained from the Council on request.)

One of the graphs in the reprint accompanying the Basmeter shows the relationship of the pulse rate to the basal metabolic rate. It indicates that, roughly, there should be an increase of about 1 per cent in the basal metabolic rate for each beat per minute increase in pulse rate. Therefore the results are indisputably in conflict with one of the supposedly sound principles behind the device.

The following are direct quotations from the text of the reprint:

"No preliminaries to the test are necessary, such as the required period of rest, omission of the morning meal, etc."

"Hypertension and other causes of high blood pressure, a rapid or slow pulse or respiratory rate due to other causes besides involvement of the thyroid, obesity, etc., do not affect the reading of the basal rate on the Basmeter. The constants (Factors J) compensate for any of these changes. No individual factor such as age, weight, blood pressure, pulse rate, and respiratory rate affect the basal metabolic rate, but the combination of all the 5 factors, in relation to the constants (Factors J), give the correct basal metabolic rate."

The Council conducted a survey covering 110 cases in which the basal metabolic rates determined by use of the Basmeter were compared with those determined by use of the Aub-Du Bois standard and/or the Harris-Benedict standard. Only in ten of these cases did the rates obtained by means of the Basmeter agree within 2 per cent with the rates obtained with the standard methods, and in many cases the variation was very great. (The tabular data are omitted from this report but will be included in a reprint which may be obtained from the Council on request.)

The great discrepancy between basal metabolic rates as determined by standard methods and by the Basmeter, as well as the obvious discontinuity of results with the changing of one physical factor, would indicate that the device is subject to errors which are paradoxical in the light of the supposedly sound principles on which the design of the device is based.

The primary source of possible deviation appears to lie in the arrangement of the figures from which the "Factors J" are derived. These factors are a series of numbers for each age

group, the individual factor being determined by the two divided by a hairline on the slide of the device, the two numbers being combined thus, for example: if the hairline lies between 3 and 2, the Factor J is 32. A sample of the series of numbers 1 2 8 3 2 4 3 7 3 1 2 shows that a slight movement of the slide, as for one pulse beat change, would change the Factor J in no sequential manner.

Consequently the Basmeter appears to be liable to errors not explicable in the relative magnitude of the change in factors which alter the calculated rates.

The Council on Physical Therapy voted not to accept the Basmeter for inclusion on its list of accepted devices.

AUREX HEARING AID ACCEPTABLE

Manufacturer: The Aurex Corporation, 1115 North Franklin Street, Chicago.

The Aurex Hearing Aid consists of three main components: (1) a microphone and amplifier assembly of rectangular shape, 5 by 2¼ by ⅝ inches in size and weighing 135 Gm., (2) a miniature crystal receiver with a molded soft rubber earpiece, which is three-fourths inch in diameter, one-fourth inch thick and weighs 10 Gm., and (3) a combination assembly of A and B batteries having a total weight of 304 Gm. The A battery current consumption is about 60 milliamperes and that of the B battery about 0.33 milliampere. The volume is controlled by a lever on the side of the microphone case.

The unit was tested in a laboratory acceptable to the Council and the following were given as the procedure and results:



Aurex Hearing Aid.

Internal Noise.—The internal noise is not objectionable when the earpiece is closely fitted in the ear. When this is not the case, the instrument is unstable when volume is more than three-fourths on. For the most efficient use the earpiece should be molded to fit each individual patient's ear. This observation can well be made of all hearing aids of the vacuum tube type in which the gain is high.

Amplification.—Amplification measurements were made audiometrically with two deaf subjects. The gain in decibels at the frequencies indicated, with the volume control set three-fourths on, is given in table 1.

TABLE 1.—Amplification with Volume Control
Three-Fourths On

Frequency	128	256	512	1,024	2,048	4,096
Amplification in decibels.....	4	4	15	22	41	5

Amplification with the instrument set at one-half volume at the normal threshold was measured by means of tuning forks of known decay rates. These values are given in table 2.

TABLE 2.—Amplification at One-Half Volume

Frequency	128	256	512	1,024	2,048	4,096
Amplification at normal threshold	None	None	19	30	33	10

It should be remarked that the gain at 4,096 cycles is very markedly affected by the tightness of the fit of the auricle in the ear cavity. The gain of 41 decibels at 2,048 cycles represents a certain degree of instability of the system with a tendency to feed back at this frequency.

The Council on Physical Therapy voted to accept the Aurex Hearing Aid for inclusion on the Council's list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JULY 6, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

PHYSIOLOGICALLY ACTIVE IODIZED PROTEINS

The synthesis of a physiologically active iodine-containing protein with a specific calorogenic effect has always been assumed to be limited to the thyroid gland. The localization of almost all the iodine of the body in the thyroid and the metabolic influence of the gland have served to emphasize the relationship of the iodine-containing compounds of the thyroid to the regulation of energy metabolism. The synthesis and the degradation of thyroglobulin have been considered to be fundamental reactions under the control of the thyroid. Now come reports of the preparation of proteins of extra-thyroidal origin which possess metabolic effects formerly considered to be restricted to the thyroid gland and to products derived from it. Perhaps this work will prove of fundamental importance in providing inexpensive and ready sources of thyroid-like hormone for therapeutic

use. The earlier reports of Abelin and his colleagues¹ presented evidence that iodized proteins, prepared in the laboratory by the treatment of a protein with iodine, exhibited physiologic activity resembling that of thyroglobulin. These investigators conducted fractionation experiments with hydrolysates of the iodized products and succeeded in concentrating the activity in an iodine-containing fraction the chemical properties of which resembled those of thyroxine concentrates obtained from thyroid tissue. As their preparation exhibited thyroxine-like activity although they were unable to establish definitely the chemical nature of the product, Abelin and his colleagues named their active fraction "homothyroxine." More recently Ludwig and von Mutzenbecher² have carefully reinvestigated and expanded the investigation of the iodine compounds present in iodized products prepared in the laboratory. The latter investigators have developed the optimal conditions for the introduction of iodine into proteins and have iodized casein, serum albumin, serum globulin, silk fibroin and edestin. From each of the products, following hydrolysis, it was possible to prepare fractions which had the property of stimulating metabolism. Furthermore, it is reported that from each preparation it was possible to isolate thyroxine by further purification. Casein appeared to give the most satisfactory product from a chemical and physiologic standpoint; the serum proteins also proved to be satisfactory starting material. From the hydrolysate of iodinated casein it was possible to isolate not only thyroxine but also mono-iodotyrosine and di-iodotyrosine.

The experiments of Ludwig and von Mutzenbecher have been confirmed in both the laboratory and the clinic by investigators who, by virtue of their previous investigations, are highly qualified in the field of thyroid chemistry and physiology. Harrington and Rivers³ have treated casein with iodine under carefully controlled conditions and have obtained a product with physiologic activity similar to that of thyroglobulin and from which crystalline thyroxine was isolated. Lerman and Salter⁴ report that by the iodination of serum protein they have prepared a product which produced successful responses in myxedema and cretinism and in thyroidectomized rabbits. In terms of total weight, the activity of the iodoprotein was approximately 20 per cent of that of whole thyroid; in terms of iodine content, the activity was about one four hundredth that of thyroid tissue. The artificially iodized product was hydrolyzed by alkali and by enzymes, and Lerman and Salter were able to prepare concentrates of iodine-containing products the chemical and physiologic properties of which resembled those of thyroxine and its derivatives.

1. Abelin, Isaak, and Florin, A.: *Arch. f. exper. Path. u. Pharmacol.* **171**: 443, 1933. Abelin, *ibid.* **175**: 146, 151, 1934; **181**: 250, 1936. Abelin, Isaak, and Nefel, A., *ibid.* **189**: 473, 1938.
2. Ludwig, W., and von Mutzenbecher, P.: *Ztschr. f. physiol. Chem.* **258**: 195 (April) 1939. von Mutzenbecher, *ibid.* **261**: 253 (Oct.) 1939.
3. Harrington, C. R., and Rivers, R. V. P.: *Nature* **144**: 205 (July 29) 1939.
4. Lerman, Jacob, and Salter, W. T.: *Endocrinology* **25**: 712 (Nov.) 1939.

The practical importance of having inexpensive sources of physiologically active iodine-containing products is self evident. The data which have been obtained on iodized proteins have been revealing and lead to a renewal of interest in some of the fundamental problems of thyroid physiology. A solution of the mechanism of the synthesis of thyroxine in the laboratory during the treatment of proteins with iodine may provide a possible answer to the question of the mechanism of the synthesis in the thyroid gland. The role of tyrosine and of di-iodotyrosine in this synthesis and the possible existence in proteins of thyroxine-like nuclei containing no iodine but which readily absorb this element are suggestive problems. These studies may ultimately shed light on still another fundamental problem of thyroid physiology: the specific nature of the thyroid hormone which is liberated by the thyroid gland into the circulation and which is the effective agent in accelerating the metabolic rate of the tissues.

INDUSTRIAL HEALTH AND NATIONAL DEFENSE

Modern warfare depends on industrial production. The skilled worker becomes of importance equal to that of the man under arms; his indispensability grows as it becomes difficult or impossible to replace him. Shortages are said to exist now in certain classifications of experienced craftsmen. The problem then is not solely one of educating new workers, since long periods of apprenticeship are necessary to acquire dependable ability. More important is the task of guarding the existing supply of competent and skilled workers against preventable disability. Fortunately, the medical and allied professions find themselves in better position now than in 1917 to combat causes of lost time in industry. Lessons learned in the last war about preventive industrial medicine, industrial hygiene engineering and industrial nursing have not been forgotten. Since that time technics for control over industrially induced accident or sickness have developed steadily. Trained personnel and special facilities for investigation and prevention are available in nearly all the industrial states, maintained by governmental agencies or by private industrial or insurance organizations and universities. They constitute the immediately available machinery for investigation of new occupational hazards and improved control over old ones.

Private industry also has equipped itself to protect its workers through the maintenance of medical departments. Physicians in charge of such departments are far more numerous now than formerly. They are a body of specialists in industrial practice whose equipment has progressed far beyond the relative immaturity of twenty-five years ago. In their responsible positions they act as sources of information and training for additional medical recruits. Already arrangements have been made to place at the disposal of the govern-

ment the knowledge and special ability of these industrial physicians and hygienists.

Similarly the general medical profession is in a much better state of organization for specific assignments in industrial health than previously. The Council on Industrial Health has acquired information about the activities of all major medical agencies interested in the health of workers. It has conducted a census of physicians who confine their interest or give special attention to industry throughout the nation. It has investigated available facilities for industrial medical training and has arrived at conclusions about what needs to be taught both before and after graduation. At the recommendation of the Council on Industrial Health, cooperating committees in the state medical societies have been formed in the industrial areas and in a great many counties. These organized units, augmented as necessary, are available for investigations on the nature and prevalence of industrial hazards, the correlation of all local resources for control of industrial absenteeism, and the utilization of channels for professional training as well as health education for the worker. Loss of working time by skilled and indispensable workers, no matter what the cause, must be classed in war time as casualties which require mobilization of medical resources for competent handling just as do those which occur in the field. The medical profession needs to be well prepared to shoulder this special responsibility.

DESOXYCORTICOSTERONE ACETATE

In last week's issue of *THE JOURNAL* appeared three papers on the treatment of Addison's disease and a statement by Dr. E. S. Gordon¹ on the therapeutic status of desoxycorticosterone acetate published under the auspices of the Council on Pharmacy and Chemistry. Our knowledge of the effectiveness of this substance and the possible dangers from indiscriminate use were clearly defined. Recently the Schering Corporation, one of the manufacturers of desoxycorticosterone acetate (Cortate), has been conducting an active advertising campaign to promote the use of this substance in the prevention and treatment of surgical shock. The arguments used seem subtle. In addition to the usual selection of the favorable references in the literature, the firm has supplied physicians with blank charts entitled "Cortate Routine" on which is presented a convenient form with specific directions for the ordering of Cortate (desoxycorticosterone acetate) preoperatively and postoperatively. Actually the clinical evidence to support claims for using desoxycorticosterone acetate in the treatment of secondary shock is scanty. A number of reports have been published on the relationship between shock and the adrenal cortex in laboratory animals. Much of this work deals with a comparison of the symptoms and signs of animals that have acute adrenal insufficiency

1. Gordon, E. S.: The Use of Desoxycorticosterone and Its Esters in the Treatment of Addison's Disease, *J. A. M. A.* **114**: 2549 (June 29) 1940.

with those in secondary shock. Both these conditions lead to blood concentration, hypotension, subnormal temperature and asthenia. It has been also indicated that adrenalectomized animals are susceptible to trauma and other injurious processes and that adrenal cortex extracts protect such animals. None of this evidence, however, should be accepted as proof that the administration of adrenal cortex preparations is of value in clinical shock.

Most of the clinical data on which the Schering firm bases its recommendation for the use of desoxycorticosterone acetate in shock appears in a report by Perla and his associates,² as yet unconfirmed, on the successful prevention of surgical shock in debilitated patients who were subjected to operation. Without any criticism of the scientific value of the report by Perla, it would appear to be hardly sufficient to sustain the claims made in promotion of the product.

Confirmation of the work of Perla and his associates with evidence supported by accurate scientific studies should be awaited before routine therapeutic use is attempted. Particularly opportune at this time is the statement by the Council that desoxycorticosterone does not furnish complete replacement therapy and the warning against the indiscriminate and excessive use of this substance in routine therapy.

Current Comment

A BUSINESSMAN'S APPEAL

In an address by Mr. J. Howard Pew, member of the Board of Trustees of Jefferson Medical College of Philadelphia, before the alumni dinner of that organization on June 6, he said in part: "I appeal to you men of the medical profession to come to the defense of our American system of free enterprise and equal opportunity, for the truth is that no economic planning authority could possibly have foreseen, planned, plotted and organized such an amazing spectacle of scientific, medical and industrial progress as the world has witnessed right here in America during this last century. No trust or combination, private or governmental, could have accomplished it. It could have been achieved only under conditions where there was wide-open opportunity for all the genius, inventive ability, organizing capacity and managerial skill of a great people." THE JOURNAL appreciates the compliment in this appeal. And we would appeal to American business to recognize that the regimentation of medicine would be the first insidious step in this country, as it has been in every other country in the world where it was established, toward a regimentation of all the actions of human beings. Eventually this leads to that descent into brutality and lack of consideration for the individual human being which characterizes all totalitarian governments.

URETERO-INTESTINAL ANASTOMOSIS

In an attempt to reduce the incidence of hydronephrosis and pyelonephrosis subsequent to implantation of the ureter into the colon, Brackin,¹ experimenting with dogs, employed intact parietal peritoneum overlying the ureter in a lateral submucous uretero-intestinal anastomosis. A necrosing suture was placed in the uretero-intestinal opening; the resulting peritoneal reaction, he says, prevents leakage and tends to localize and absorb postoperative infection. The procedure was successfully accomplished in fifty-two experimental implantations in animals, after each of which a tissue necrosis occurred which resulted in a ureterosigmoidal anastomosis. In ten consecutive bilateral implantations in healthy dogs, pathologic changes in the kidneys or in the ureters were not apparent at necropsy after periods varying from three weeks to eleven months. In three animals, which died of extensive bronchial pneumonia within five days after the initial transplantation, bilateral pyelonephritis was observed. As brought out in the discussion of this paper by Walters, the difference between this type of transplantation in dogs and in human beings is significant. Since there is as yet insufficient clinical evidence of the applicability of this procedure in man, caution should be observed in applying it clinically.

PHYSIOLOGY OF CONCUSSION

It is generally agreed among fighters in the ring that it is easier to knock out an opponent by hitting a point on the lower jaw than by any other blow to the head, although it is possible by a more forceful blow to knock an opponent unconscious with a blow to almost any region of the head. In an attempt to elucidate certain aspects of the physiology of concussion, Scott¹ succeeded in demonstrating in dogs a method for recording changes in intracranial pressure produced by a blow to the head. A blow of sufficient force to cause unconsciousness results in a rise in intracranial pressure considerably above that of the systolic blood pressure. After the blow the intracranial pressure returns to the normal level and remains there. Furthermore, a loss of consciousness occurs in the dog when the intracranial pressure is raised to a level above that of the arterial blood pressure even though this pressure is maintained for only one second. Scott also demonstrated that, when the intracranial pressure does not exceed the systolic blood pressure, loss of consciousness does not occur even though the lower intracranial pressure is maintained for as long as thirty minutes. As a result of these studies, Scott feels that loss of consciousness as a result of a blow on the head may possibly be explained on the basis of short lasting, complete cerebral anemia, and he points out that this concept agrees with the previous work of Cannon and of Weiss and Baker. He further suggests that the syndrome which is known as "punch drunk" may be the result of damage to the central nervous tissue from cumulative anoxia caused by repeated, short lasting anemias produced in this manner.

2. Perla, David; Freiman, D. G.; Sandberg, Marta, and Greenberg, S. S.: Prevention of Nistamine and Surgical Shock by Cortical Hormone (Desoxycorticosterone Acetate and Cortine) and Saline, *Proc. Soc. Exper. Biol. & Med.* 43: 397 (March) 1940.

1. Brackin, R. E.: A New Method of Uretero-Intestinal Anastomosis Utilizing Peritoneum, *Arch. Surg.* 40: 658 (April) 1940.
1. Scott, W. W.: Physiology of Concussion, *Arch. Neurol. & Psychiat.* 43: 270 (Feb.) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

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HEALTH AND MEDICAL PREPAREDNESS

THOMAS PARRAN, M.D.

Surgeon General, U. S. Public Health Service
WASHINGTON, D. C.

The problem which concerns each of us today is what we can do to contribute to the safety of our country. Traditionally, as doctors and nurses, we have been servants of peace. When war did come, it was our job to patch up the wounds, ease the suffering of the wounded, and repair as best we could the damage done by shot and shell.

We are not at war. If we have time enough—if we are swift and wise enough in the time that we have—war in this hemisphere may be prevented. But the old rules of war, and the preparation for it, have been demolished. The whole task of national defense is different from what it was twenty-five years ago. Just as the perversion of the physical and chemical sciences has brought more brutal, more rapid, more devastating destruction both to unprepared armies and to unarmed civilians, the developments of the medical sciences have expanded the scope of what doctors and public health workers can do for preparedness. The concept of a total war necessitates the concept of a total defense—a total national effort not only toward resistance but toward unassailable strength.

Psychologically, this country as yet seems unprepared for the total effort toward strength which recent world events make imperative. On the one hand we hear imprecations because we are not now better prepared in guns and ships and planes and organized manpower. On the other hand we hear criticism at steps taken now to prepare promptly against aggression toward ourselves or our immediate neighbors. One of the risks I see to national unity of action lies in the idea that defensiveness alone is all that we need to preserve our democracy. Yet, as Governor Lehman has said again and again, democracy is a thing we must constantly fight for. All recorded history shows, I think you will agree, that no nation has arisen to strength, as we have, or remained strong, as we hope to—no human rights have been established or liberties maintained—without dynamic, aggressive action. Saint Paul and the apostles were not defensive when they established the Christian faith. Our Revolutionary

ancestors were not defensive when they fought to establish human liberties and found a nation. The Boston tea party, for example, was one of the most provocative acts on record. Buchanan was merely defensive when he permitted the nation to fall into the turbulence and dissension which preceded the Civil War. Lincoln took the dynamic aggressive to preserve the Union, without which we now should be as helpless as little Denmark.

REQUISITES FOR BUILDING UP NATIONAL STRENGTH

Today I would discuss with you the aggressive action which you and I, by virtue of our calling—because we are the servants of peace—must take to build up national strength. The needs to be met are enormous in scope yet simple in analysis. National strength can be built up only by the adequate application of all the sciences to the provision of armament, munitions and supplies, food and manpower. Our job is manpower.

Seven competent, trustworthy persons recently were called to assist the government in national defense. Industry is represented both in raw materials and in processing. Labor, agriculture, transportation, the consumer are represented. There is a shrewd eye on the stabilization of prices. Research problems in the physical and chemical sciences are being attacked with vigor by an able committee, which will apply all the knowledge we have or can discover to the perfection of armaments. Yet so far as I know there has been no more thought than in 1917 of the application of medical and public health science to the physical problems of a nation arming.

Yet for what cause is this nation arming if not on behalf of the men, women and children who compose it? Their physical fitness, their freedom from preventable disease, their morale or mental stamina, will determine almost entirely the effectiveness of all other defense efforts. Important in the easy days of peace without a cloud on the horizon, it is urgent now that the people of this nation be physically tough, mentally sound and morally strong. If we are not, to quote Mr. MacLeish, "we can leave our planes unbuilt and our battleships on paper. We shall not need them."

In time of stress, the health problems of the military and civilian population are inseparable. At present they are the responsibility of many unrelated federal agencies having the happiest personal good will toward one another but with no more official authority or compulsion toward coordinated action than did an airplane factory and an automobile plant two months ago. Each of these agencies legally can perform only certain functions set up by law. Each needs a closer working integration with the organized medical and public health profession. The state health departments are as diverse as the forty-eight states. None of the official agencies have the benefits of a full working relationship with the great voluntary associations for health and welfare in which doctors, dentists, nurses, engineers, in their technical capacity, work side by side with citizens to caulk up the leaks in the hull of our national man-

power. Not one of the official agencies has the full aid and service which the public spirited foundations set up to promote health and welfare are able to give.

TASKS FOR A COORDINATOR

Our defense plans, for the immediate emergency, are still young. There is much in the way of organization and coordination yet to come. But as a first step in meeting the vital needs of manpower preparedness I propose that a coordinator of medical and health preparedness for national defense be appointed under the National Defense Council. There is much for him to do. He would work with and through the Surgeon Generals of the U. S. Army, the U. S. Navy and the U. S. Public Health Service, other federal agencies, the National Research Council and the national voluntary organizations concerned with the prevention, diagnosis and treatment of disease.

A first task is the need for listing and classifying professional and technical personnel in the country; for planning and aiding, if and when necessary, the recruitment and mobilization of medical and health personnel.

Another urgent task involves the protection and promotion of the health of industrial workers. With the vast expansion of the war industries, many new industrial hazards appear and familiar ones are intensified. When new factories are designed, expert industrial hygiene advice is required for proper installation of power exhausts of chemical gases. Records of present performance show the need of extended industrial hygiene measures to control and prevent special health hazards. In the recruitment and training of workers, thorough physical examinations are necessary on employment and periodically thereafter. It is wasteful for industry to train a highly skilled employee over long months, only to have him break down suddenly with tuberculosis, mental disease or some other crippling condition. The expansion of war industries will bring acute problems of housing, medical care and health protection for workers and their families. Our industrial machines are the most efficient in the world. The men and women who man the machines must have a comparable efficiency.

DISEASES AND THEIR CONTROL

Certain diseases have particular military importance. The venereal diseases are at the top of the list. They caused more disability in the last war than anything except wounds and influenza. Fortunately we have been forehanded in building some machinery in every state to deal with this problem. We need to intensify these efforts, especially in areas of military and industrial mobilization.

The importance of tuberculosis is accentuated by the current situation. Here too we have made some progress since the last war in terms of a lower active infection rate and a lower death rate, but we do not have in any state the machinery to detect all active cases of the disease. In very few states do we have the sanatoriums to care for such cases. It should be possible promptly to find and to isolate all sources of infection. Recent developments in the small and microfilm techniques mean that we can easily afford it.

Not one of the seven fine persons on the National Advisory Commission of the Defense Council, however, is aware of what this country can do to eliminate tuberculosis as a major obstacle to national security. We know that Hitler has put all of his active tuberculosis together in factories to give—between dying coughs—a few months of service in munition making.

This was segregation and service to the state without regard for the welfare of the individual. If we plan well now, we shall not need such suicide squads for bomb manufacture. Segregate, yes; but let us restore also.

Of the many military medical and health problems in the tropical Americas, the most important is malaria. There is no disease of comparable importance (except the mental diseases) against which we have made less scientific progress during my generation. Quinine is still the major remedy. Like rubber, originally secured from South America, now our major source of supply is from across the Pacific Ocean—the Netherland East Indies. The Netherlands is no longer able to import, process and distribute this remedy. Its cartel prevented us from storing a sufficient war chest of our most needed medical strategic material. All of Central and South America now look to us to supply their needs. For two years I have been concerned with this problem. It is not yet solved. No major military operations in the tropics of this hemisphere are possible without quinine or the equally potent German synthetic, atabrine. Here is another job for a national coordinator on the medical front.

Another strategic medical material, for which we are dependent on foreign sources, is opium. For four years I have prescribed the total annual amounts which could be imported into the United States. Before and after Munich I aided our commercial importers to build up a war chest of opium and morphine. In the vaults at Washington, formerly used to store gold, we have stored enough morphine for at least three years. Our regular source has been from the eastern Mediterranean, now closed. Before this supply is exhausted we can if necessary grow in certain areas of the United States the pain relieving poppy plant. But it must be planned now.

Other diseases require our attention. Next to the venereal diseases, mumps is the most disabling of the acute infections among recruits. Meningitis was a great hazard during the last war. Influenza still is a major threat. During the intervening twenty-two years, many facts about it are becoming clear; but, with present knowledge, effective prevention and control are not possible. Research must be speeded up and coordinated. It may be that the nation which first learns how to control influenza will by this knowledge tip the scale toward victory in the wars ahead. No one now is coordinating our search for the practical prevention of this major hazard to successful defense. Until recent months we could expect aid from medical discoveries in our sister democracies. Now in this country alone we must carry the burden. As yet we have not gone forward with it.

When armies are mobilized, certain proved immunizations are used. Typhoid fever, yes. Smallpox, yes—since Jenner's discovery of more than a hundred years ago. A recently developed toxoid against tetanus is of proved value and will be used as a routine. Effective immunization against gas gangrene would be another great aid. By a few months of coordinated effort on the part of commercial, university and governmental groups, a practical protection against this major war hazard should be perfected. Here is another job for the coordinator.

Our first concern may be in tropical America. I have discussed malaria. What about yellow fever? Prevalent throughout large areas of South America, a constant threat to the southern half of the United States, we do

not have in this country enough of the effective vaccine against it to immunize one regiment! In spite of requests from year to year, I have not been able to secure funds with which to produce a reserve supply.

These examples, among many that I could cite, illustrate my major thesis. There are many diseases, of great military importance, which we could control if we were given the will, the authority and the money to do it.

If or when war comes, every million men mobilized need 7,500 doctors drawn from civil practice. Dentists, nurses, sanitary engineers are needed too. In the mobilization of four million during the last war, more than a fourth of the effective medical men of the country were called to the colors. Whole counties were depleted of doctors. Many medical schools were almost put out of business, because the best men left for military duty. We should not repeat these mistakes. Today we should investigate who should go, who should stay to practice, to teach, to operate an essential civilian service. We have no machinery now to do this. A coordinator of medical and health preparedness should create the machinery, working with the public health agencies, the schools and the medical profession itself.

We have a shortage of laboratory technicians. Intensive courses would provide more. Universal training would deplete the ranks of medical students; yet we need doctors each year to replace obsolescence. Some medical and other scientists are vastly more valuable to the country working on their present jobs than they possibly could be in the Army or Navy. Here are other tasks for medical planning through a coordinator.

There is urgent need for standardization of many medical and surgical procedures for emergency application in time of war. Much wasted effort also could be saved through standardization of medical equipment which would be of value in civilian no less than in military practice.

THE PROBLEM OF NATIONAL FITNESS

Further, let us consider the whole problem of national fitness. The President has recommended that all youth give one year to public service—he trained during this time in some skill. How fit are they from a physical and mental point of view? Enrolment should include a careful examination. All correctable defects should receive prompt attention. As yet there is no organization, no planning of an organization to do it. This is a task projected.

Let us consider two tasks immediately before us. The National Youth Administration employs 300,000 young people. Here is a measurable group, beneficiaries of the government. After five years no plan has been worked out to appraise their physical status. Shouldn't we take this group of underprivileged youth and apply our proved medical science to relieve their correctable defects?

Employed by the Works Projects Administration are nearly two million people. The nation wants to use their services; they themselves want to serve in the ways they can best contribute to national safety. What is their physical status? No one knows. I propose that each of them be examined; that we use methods comparable to those of the draft boards of twenty-two years ago and classify the Works Projects Administration employees physically into three or four classes. Those qualified to become good workmen should be first on the list for training in the industries now short handed. Those who have remediable defects merit rehabilitation. Up to now no agency has had the authority or the

money to do these two specific jobs, which seem important in national preparedness.

If our workers are malnourished, they cannot be efficient in producing what we need for defense. Yet every survey of nutrition, by whatever method conducted, shows that malnutrition in this country is widespread and serious. For example, studies by the Department of Agriculture show that 40 per cent of the people are not getting a diet adequate to maintain good health and vigor. Eight out of every ten in this category do not have an income sufficient to purchase, at market prices, a diet adequate in amount and kind; this in spite of the fact that the foods of which the nation has an apparent surplus are those in which the dietary of so many is deficient—milk and milk products, citrus fruits, green vegetables and meat.

Not through any pity for their working people, but because their scientists proved to them that it was an essential to national power, the Germans began several years ago to provide for the working masses a diet better than ours have now. We have made a beginning in this direction through the food stamp plan. What we need is an intensive national drive, with rigid scientific controls, to use the food we have to improve the fitness of our manpower.

Though I would not presume to draw up a blueprint for the whole effort of health preparedness, each of the problems mentioned needs prompt attention. With authority from the National Defense Council, several committees of experts, both official and professional, should undertake special responsibilities. What seems now a huge, illimitable job is, in reality, a composite of measurable tasks. There is a competent person to do each, if it is assigned to him. There is the will among our professions and among our citizens which will see that each is done. But, I repeat, the first step is a strong leader in the National Defense Council to see that the country's needs are met for physical and mental preparedness, for health and medical mobilization, for peace or war. At the same time he would serve to unite the efforts of official professional, commercial and voluntary groups in our unified drive for aggressive strength.

IMMEDIATE TASK OF MEDICAL SCIENCE

In the past there have been division of opinion and occasional dissension among our professions concerning methods proposed to bring better health and a higher standard of medical care to our people. In the face of danger it is the democratic way—even the herd instinct—to unite for the agreed objectives of safety. We cannot now afford controversies. The preparedness of our manpower for national safety is not controversial. Given a hand in the planning, all of us together, official and professional, can work out methods in which we all believe.

There is no time for dogged adherence to outworn patterns or for a major change in proved forms of medical practice. Medical science grows, expands, opens up new possibilities for saving life and building strength. In the application of its basic sciences, medical practice must expand also to meet the new demands of the nation for self preservation.

In the dictatorships, the state is served by sacrifice of the individual and enslavement of the men of science. If our democracy is to stand, we—as doctors, as health officers, as health workers, as citizens—of our own free will, because we know it is necessary, must put medical science to work now, fully, to make our men as good as our machines.

ORGANIZATION SECTION

PROCEEDINGS OF THE NEW YORK SESSION

MINUTES OF THE NINETY-FIRST ANNUAL SESSION OF THE AMERICAN MEDICAL ASSOCIATION, HELD IN NEW YORK, JUNE 10-14, 1940

MINUTES OF THE SECTIONS

SECTION ON PRACTICE OF MEDICINE

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2:10 by the chairman, Dr. William S. McCann, Rochester, N. Y.

Dr. Bayard T. Horton, Rochester, Minn., read a paper on "The Use of Histamine in the Treatment of Specific Types of Headaches." Discussed by Drs. Emanuel Libman, New York; Leonard G. Rowntree, Philadelphia, and Bayard T. Horton, Rochester, Minn.

Drs. James A. Greene, L. W. Swanson and Carl A. Jacobs, Iowa City, presented a paper on "The Relation of Control of Diabetes Mellitus to the Healing of Clean and Infected Wounds and to the Incidence of Infection in Clean Wounds." Discussed by Drs. Elliott P. Joslin, Boston; Roy D. McClure, Detroit, and James A. Greene, Iowa City.

Dr. Elliott P. Joslin, Boston, read the Frank Billings Lecture on "The Universality of Diabetes." Dr. Joslin was introduced by Dr. Walter L. Biering of Des Moines, Iowa, who gave a brief historical review of the Frank Billings lectures of previous years.

Drs. Ernest E. Irons and Carl W. Apfelbach, Chicago, presented a paper on "Aspiration Bronchopneumonia with Special Reference to Aspiration of Stomach Contents." Discussed by Drs. J. P. Simonds, Chicago; William J. Kerr, San Francisco, and Carl W. Apfelbach, Chicago.

The following papers were read as a symposium on "Pulmonary Tuberculosis":

Dr. J. Arthur Myers, Minneapolis: "Epidemiology of Pulmonary Tuberculosis."

Dr. Hugh M. Kinghorn, Saranac Lake, N. Y.: "Diagnosis of Pulmonary Tuberculosis."

Dr. Ralph C. Matson, Portland, Ore.: "Treatment of Pulmonary Tuberculosis."

These three papers were discussed by Drs. Ruth E. Boynton, Minneapolis; Louis Hamman, Baltimore, and Alexius M. Forster, Colorado Springs, Colo.

THURSDAY, JUNE 13—AFTERNOON

The following officers were elected: chairman, Dr. Fred M. Smith, Iowa City; vice chairman, Dr. W. W. Palmer, New York; secretary, Dr. William D. Stroud, Philadelphia; delegate, Dr. James E. Paullin, Atlanta, Ga.; alternate, Dr. Ernest E. Irons, Chicago; member of the American Board of Internal Medicine, Dr. Reginald Fitz, Boston.

Dr. John S. Lawrence, Rochester, N. Y., read a paper on "Leukopenia: A Discussion of Its Various Modes of Production." Discussed by Drs. George R. Minot, Boston; Russell L. Haden, Cleveland, and John S. Lawrence, Rochester, N. Y.

Dr. William S. McCann, Rochester, N. Y., read the Chairman's address, entitled "Orthostatic Hypertension: The Effect of Nephropathy on the Renal Blood Flow."

Drs. Harry Walker and William B. Porter, Richmond, Va., presented a paper on "The Clinical Syndrome Associated with

Intercapillary Glomerulosclerosis." Discussed by Drs. Soma Weiss, Boston; Paul Kimmelstiel, Richmond, Va.; Sheppard Siegal, New York, and William B. Porter, Richmond, Va.

Drs. Frederick A. Willins and J. P. English, Rochester, Minn., presented a paper on "The Relation of the Use of Tobacco to Coronary Disease." Discussed by Drs. Francis D. Murphy, Milwaukee; George R. Hermann, Galveston, Texas; Soma Weiss, Boston; William D. Stroud, Philadelphia, and Frederick A. Willins, Rochester, Minn.

Drs. N. C. Gilbert, G. K. Fenn and G. V. LeRoy, Chicago, presented a paper on "The Effect of Distention of Abdominal Viscera on the Coronary Flow and on Angina Pectoris." Discussed by Drs. Lester M. Morrison, Philadelphia; C. W. Greene, Stanford University, Calif., and H. R. Miller, New York.

Drs. Herrman L. Blumgart, Monroe J. Schlesinger and Paul M. Zoll, Boston, presented a paper on "Clinical and Pathologic Studies in Coronary Artery Disease." Discussed by Drs. Fred M. Smith, Iowa City; William D. Stroud, Philadelphia, and Herrman L. Blumgart, Boston.

FRIDAY, JUNE 14—AFTERNOON

A joint meeting was held with the Section on Pharmacology and Therapeutics. The proceedings are reported in the minutes of that section.

SECTION ON SURGERY, GENERAL AND ABDOMINAL

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman, Dr. Thomas M. Joyce, Portland, Ore.

Drs. Edwin M. Miller and E. H. Fell, Chicago, and Clayton E. Brock, St. Louis, presented a paper on "Acute Appendicitis in Children: A Clinical Study of More Than 1,000 Cases."

Drs. Edward S. Stafford and David H. Sprong Jr., Baltimore, presented a paper on "An Analysis of the Mortality Resulting from Acute Appendicitis in the Johns Hopkins Hospital."

Drs. D. Woolfolk Barrow, Lexington, Ky., and Alton Ochsen, New Orleans, presented a paper on "The Treatment of Appendical Peritonitis."

These three papers were discussed by Drs. Alton Ochsen, New Orleans; E. H. Fell, Chicago; Harvey B. Stone, Baltimore; John S. Horsley Jr., Richmond, Va.; John J. Gilbride, Philadelphia, and Edwin M. Miller, Chicago.

Drs. Charles C. Lund and John H. Crandon, Boston, presented a paper on "Experimental Scurvy and Ascorbic Acid Deficiency in Surgical Patients."

Drs. John B. Hartzell, James M. Winfield and J. Logan Irvin, Detroit, presented a paper on "Plasma Vitamin C and Serum Protein Levels in Wound Disruption."

These two papers were discussed by Drs. Thomas T. Mackie, New York; Jonathan Rhoads, Philadelphia; Marshall K. Bartlett, Boston; Charles C. Lund, Boston, and John B. Hartzell, Detroit.

Dr. Elkin L. Rippey, Nashville, Tenn., read a paper on "Perforating Gunshot Wounds of the Abdomen."

Drs. Harold Price Totten and J. Norman O'Neill, Los Angeles, presented a paper on "Subcutaneous Injuries of the Abdomen."

These two papers were discussed by Drs. Adolph A. Walking, Philadelphia; Walter E. Lee, Philadelphia; Thomas M. Joyce, Portland, Ore.; R. Arnold Griswold, Louisville, Ky.; Leo Eloesser, San Francisco; Harry E. Mock, Chicago; J. Norman O'Neill, Los Angeles, and Elkin L. Rippey, Nashville, Tenn.

THURSDAY, JUNE 13—MORNING

The following officers were elected: chairman, Dr. Lloyd Noland, Birmingham, Ala.; vice chairman, Dr. Thomas E. Jones, Cleveland; secretary, Dr. Arthur W. Allen, Boston; delegate, Dr. Fred W. Rankin, Lexington, Ky.; alternate, Dr. Hugh H. Trout, Roanoke, Va.; member of the Board of Governors, American College of Surgeons, W. Barclay Parsons, New York; member of the Board of Neurosurgery, Dr. Byron Stookey, New York.

Drs. Reed M. Nesbit and Rigdon K. Ratliff, Ann Arbor, Mich., presented a paper on "Hypertension Associated with Unilateral Kidney Infection." Discussed by Drs. E. Granville Crabtree, Boston; George W. Fish, New York; Henry A. Schroeder, New York, and Reed M. Nesbit, Ann Arbor, Mich.

Dr. Frank K. Boland, Atlanta, Ga., read a paper on "Morsus Humanus." Discussed by Drs. Michael L. Mason, Chicago; Frank L. Meleney, New York; Claude E. Welch, Boston, and Frank K. Boland, Atlanta, Ga.

Dr. Thomas M. Joyce, Portland, Ore., read the chairman's address, entitled "Combination of Old and New Methods in Repair of Inguinal Hernia."

Drs. Carrington Williams and Paul Kimmelstiel, Richmond, Va., presented a paper on "Syphilis of the Stomach." Discussed by Dr. Karl A. Meyer, Chicago.

Dr. Howard K. Gray, Rochester, Minn., read a paper on "Cancer of the Stomach with Particular Reference to the Significance of Persistent Symptoms Ascribed to the Stomach and the Malignant Potentiality of Gastric Ulcers."

Drs. Carl L. Hoag and John B. deC. M. Saunders, San Francisco, presented a paper on "Jejunoplasty for Obstruction Following Gastro-Enterostomy or Subtotal Gastric Resection."

These two papers were discussed by Drs. Alton Ochsner, New Orleans; W. Barclay Parsons, New York; Arthur W. Allen, Boston; E. E. Munger, Spencer, Iowa; Howard K. Gray, Rochester, Minn., and Carl L. Hoag, San Francisco.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Orthopedic Surgery.

Dr. John H. Powers, Cooperstown, N. Y., read a paper on "Automobile Accidents in a Rural Area Traversed by a Transcontinental Highway." Discussed by Drs. Alan DeForest Smith, New York, and John H. Powers, Cooperstown, N. Y.

Drs. James S. Spced and Harold B. Boyd, Memphis Tenn., presented a paper on "Treatment of Fractures of the Ulna with Dislocation of the Head of the Radius." Discussed by Drs. Herman F. Johnson, Omaha; Benjamin Franklin Buzby, Camden, N. J.; G. Mosser Taylor, Los Angeles; J. Albert Key, St. Louis, and Harold B. Boyd, Memphis, Tenn.

Drs. Harold C. Voris, Adrien Verbrugghen and Jerry J. Kearns, Chicago, presented a paper on "Head Injuries." Discussed by Drs. S. Bernard Wortis, New York; Donald Munro, Boston; John P. Stump, New York, and Harold C. Voris, Chicago.

Dr. Joseph S. Barr, Boston, read a paper on "The Treatment of Fracture of the External Tibial Condyle (Bumper Fracture)." Discussed by Drs. Carl E. Badgley, Ann Arbor, Mich.; Earl D. McBride, Oklahoma City, and Joseph S. Barr, Boston.

Dr. Rufus H. Alldredge, New Orleans, read a paper on "Diastasis of the Distal Tibiofibular Joint and Associated

Lesions." Discussed by Drs. Clay Ray Murray, New York; George O. Eaton, Baltimore, and Rufus H. Alldredge, New Orleans.

SECTION ON OBSTETRICS AND GYNECOLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Ludwig A. Emge, San Francisco.

Drs. Richard D. Bryant and John Gwyn Fleming, Cincinnati, read a paper on "Veratrum Viride in the Treatment of Eclampsia." Discussed by Drs. Henry Lynde Woodward, Cincinnati; J. I. Hofbauer, Cincinnati, and Richard D. Bryant, Cincinnati.

The following papers were read as a symposium on "Post-pituitary Preparations in Obstetrics":

Drs. Samuel R. M. Reynolds, Brooklyn, and Douglas Power Murphy, Philadelphia: "Uterine Responses to Posterior Pituitary Substance at Term: Physiologic Considerations." Discussed by Drs. Richard Torpin, Augusta, Ga., and Sprague H. Gardiner, Baltimore.

Dr. John A. Sharkey, Philadelphia: "Should Solution of Posterior Pituitary Be Used in the First and Second Stages of Labor?" Discussed by Dr. Albert B. Davis, Camden, N. J.

Dr. George F. Pendleton, Kansas City, Mo.: "The Abuse of Solution of Posterior Pituitary During Labor." Discussed by Dr. James K. Quigley, Rochester, N. Y.

Dr. Joseph B. De Lee, Chicago: "Solution of Posterior Pituitary in Modern Obstetric Practice." Discussed by Drs. E. D. Plass, Iowa City, and E. L. King, New Orleans.

These four papers were discussed also by Drs. Douglas Power Murphy, Philadelphia; J. I. Hofbauer, Cincinnati; Rudolph W. Holmes, University, Va.; Samuel R. M. Reynolds, Brooklyn; John A. Sharkey, Philadelphia; George F. Pendleton, Kansas City, Mo., and Joseph B. De Lee, Chicago.

THURSDAY, JUNE 13—AFTERNOON

The following officers were elected: chairman, Dr. Norman F. Miller, Ann Arbor, Mich.; vice chairman, Dr. Willard R. Cooke, Galveston, Texas; secretary, Dr. Philip F. Williams, Philadelphia; representatives on American Board of Obstetrics and Gynecology, Dr. Robert D. Mussey, Rochester, Minn.; Dr. Louis E. Phaneuf, Boston, and Dr. Ludwig A. Emge, San Francisco.

Dr. Carl Henry Davis, Wilmington, Del., read a paper on "The Obstetric Forceps."

Drs. Preston T. Brown and John W. Pennington, Phoenix, Ariz., presented a paper on "Pelvic Pain of Urinary Tract Origin." Discussed by Drs. Guy L. Hummer, Baltimore, and I. W. Kahn, New York.

Drs. Gerald W. Gustafson and George J. Garceau, Indianapolis, presented a paper on "The Obstetric History of 175 Cases of Spastic Cerebral Paralysis." Discussed by Dr. Ward F. Seeley, Detroit.

Dr. B. Z. Cashman, Pittsburgh, read a paper on "The Role of Deep Cauterization in the Prevention of Cancer of the Cervix: A Report of 10,000 Cases." Discussed by Drs. Frederick C. Holden, New York; L. M. Randall, Rochester, Minn.; John J. Gilbride, Philadelphia; Morton Levin, Albany; Robert L. Dickinson, New York, and Guy L. Hummer, Baltimore.

Drs. A. N. Arneson, St. Louis, and Harry Hauptman, Jersey City, N. J., presented a paper on "Radiation in the Treatment of Carcinoma in the Body of the Uterus." Discussed by Dr. William P. Healy, New York.

Dr. Ludwig A. Emge, San Francisco, read the chairman's address, entitled "Present Trends of Socialization of Medicine in Relation to Maternal Welfare."

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Pediatrics. The proceedings are reported in the minutes of that section.

SECTION ON OPHTHALMOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman, Dr. Harry S. Gradle, Chicago.

Dr. Harry S. Gradle, Chicago, read the chairman's address.

Dr. Edward C. Ellett, Memphis, Tenn., read a paper on "Unilateral Exophthalmos."

On motion duly seconded and carried, the following resolution was adopted by the section:

WHEREAS, One state delegation has presented a resolution to the House of Delegates; and

WHEREAS, Other state medical associations have sent their recommendations direct to the section office; and

WHEREAS, The Section on Ophthalmology has been fully conscious of the needs for a new appraisal of the entire field of conservation of vision; and

WHEREAS, The House of Delegates is the legislative body of the American Medical Association; therefore, be it

Resolved, That the Section on Ophthalmology does hereby petition the House of Delegates to approve of the appointment of a Committee for the Conservation of Vision and Prevention of Blindness.

The following resolution was presented and, after discussion, was voted on and not adopted:

In view of the fact that in many parts of the country the wholesale dispensing of opium has increased suddenly and, on receipts given to the patient, that he is acting as the agent of the author of the prescription, the Section on Ophthalmology of the American Medical Association hereby approves of this method, which eliminates the secrecy of participation.

Drs. Frederick H. Verhoeff, Boston, and G. Victor Simpson, Washington, D. C., presented a paper on "Tubercle Within Central Retinal Vein, Hemorrhagic Glaucoma; Periphlebitis Retinalis in Other Eye." Discussed by Drs. Jonas S. Friedenwald, Baltimore; Arthur J. Bedell, Albany, N. Y.; Edward Jackson, Denver, and Frederick H. Verhoeff, Boston.

Dr. William L. Benedict, Rochester, Minn., read a paper on "Sclerocorneal Trephining." Discussed by Drs. Algernon B. Reese, New York; Mammel U. Troncoso, New York; H. Maxwell Langdon, Philadelphia; Benjamin Rones, Washington, and William L. Benedict, Rochester, Minn.

Drs. Cecil S. O'Brien and James H. Allen, Iowa City, presented a paper on "Unusual Changes in the Retinal Veins in Diabetes Mellitus." Discussed by Drs. Parker Heath, Detroit; Edward R. Thomas, Dayton, Ohio; Arthur J. Bedell, Albany, N. Y., and James H. Allen, Iowa City.

Dr. H. Maxwell Langdon, Philadelphia, read a paper on "Operations for Detachment of the Retina with Special Reference to the Use of the Thermophore." Discussed by Drs. Luther C. Peter, Philadelphia; John H. Dunnington, New York; Clyde Clapp, Baltimore; Lawrence Post, St. Louis; Oscar Wilkinson, Washington, D. C.; Harold F. Wabman, Los Angeles, and H. Maxwell Langdon, Philadelphia.

THURSDAY, JUNE 13—MORNING

Executive Session

Dr. Derrick Vail, Cincinnati, read a letter from Paris stating that field glasses were urgently needed by the French army for the purpose of distinguishing parachutists.

Dr. Derrick Vail, Cincinnati, reported that last fall a questionnaire was sent to the Fellows dealing with two resolutions regarding the optometrists and their relationship with ophthalmologists. The first resolution dealt with the ethics of the problem. The vote on that resolution to repeal was 96 and against repeal 480.

The second resolution dealt with (1) employment of optometrists by hospitals, (2) association of the members of the section with those of the optical trade, and (3) instruction of students of optometry by ophthalmologists. The vote on that resolution to repeal was 82 and against repeal 494. The executive committee of the section recommended that a subcommittee from the American Committee (Joint) on Optics and Visual Physiology be authorized to make a study and return a report with recommendations of a survey in the field of medical and non-medical refraction.

Dr. Arthur J. Bedell, Albany, N. Y., moved that the section proceed with the action designated. The motion was seconded, voted on and carried.

Dr. Arthur J. Bedell, Albany, N. Y., reported that the resolution passed at the Wednesday morning session had been presented to the Board of Trustees, which requested the following addition to the resolution: "Who shall be responsible to the Board of Trustees of the American Medical Association. It shall collect data showing the status of conservation measures in each state; shall act as a clearing house for all information regarding conservation of vision and prevention of blindness but shall make no pronouncement on policy or rules until approved by this section."

On motion, duly seconded, the amendment was adopted.

Dr. Albert C. Snell, Rochester, N. Y., read the report of the Committee on Visual Economics, with the following recommendations:

1. That the committee be continued and that its membership be increased to three.

2. That the committee be requested to revise the report of 1925 and that a revised report be prepared, published and sent to all members of this section one month before the next annual meeting, and that the revision be made a matter of special consideration at the 1941 meeting. The report was adopted.

Dr. Walter B. Lancaster, Boston, read the report of the American Committee (Joint) on Optics and Visual Physiology (representing the Section on Ophthalmology of the American Medical Association). The report was accepted.

Dr. Parker Heath, Detroit, Treasurer, read the report of the Committee on Knapp Testimonial Fund. The report was accepted.

Dr. Frederick H. Verhoeff, Boston, reported for the Committee on Awarding the Knapp Medal as follows: Including the first award in 1914, the Knapp Medal has been awarded only seven times in the past twenty-six years. It is evident, therefore, that previous committees have attempted to set a very high standard for subsequent papers to compete against. Each member of the present committee, justly or unjustly, has been awarded the medal, and this fact, for reasons that need not be specified, raised the hurdle to be surmounted by the papers read last year. In spite of these facts, the committee found the paper to be of immensely high merit. The committee unanimously and without any hesitation decided that one paper in every respect not only met but exceeded its requirements. This was the paper entitled "Primary Tumors of the Optic Nerve (A Phenomenon of Recklinghausen's Disease)" written by Dr. Frederick Allison Davis, Madison, Wis. Dr. Davis accepted the medal and expressed his appreciation.

Dr. Derrick Vail, Cincinnati, read the report of the Committee on National Museum of Ophthalmic Pathology. The report was accepted.

Dr. Derrick Vail, Cincinnati, read the report of the Exhibit Committee of the Section. The report was accepted.

Dr. Arthur J. Bedell, Albany, N. Y., reported as delegate of the section to the House of Delegates.

Dr. S. Judl Beauf, Portland, Maine, read the report of the Committee on American Ophthalmology.

Dr. Derrick Vail, Cincinnati, read the report of the Committee on Museum of Ophthalmic History.

The report of the Committee on American Orthoptic Council was read by Dr. Derrick Vail, Cincinnati, the chairman.

Dr. William L. Benedict, Rochester, Minn., reported for the Advisory Committee on Student Health Council that a specially designed vision test chart holder had been approved for the use of the Eye Health Committee in examination of college students; that a complete record system for the recording of results of examination of the eyes of college students made under the auspices of the Eye Health Committee had been approved and is now in operation in all colleges that belong to this organization. The committee recommended that it be continued. The report of the committee was accepted.

Dr. Parker Heath, Detroit, read the report of the Committee on Ophthalmic Literature. The report was accepted, with the recommendation that the committee be continued.

The following committee for awarding the Knapp Medal for 1940 was elected from the floor: Dr. Walter B. Lancaster, Boston; Dr. Sanford R. Gifford, Chicago, and Dr. Edward Samuel, New York.

The following officers were elected: chairman, Dr. Albert C. Snell, Rochester, N. Y.; vice chairman, Dr. Edwin M. Neher, Salt Lake City; secretary, Dr. Derrick Vail, Cincinnati; executive committee: Dr. S. Judd Beach, Portland, Maine; Dr. Harry S. Gradle, Chicago, and Dr. Albert C. Snell, Rochester, N. Y.; delegate, Dr. Arthur J. Bedell, Albany, N. Y.; alternate, Dr. Shaler A. Richardson, Jacksonville, Fla.

The following committee appointments were recommended by the executive committee and approved:

Reelection for three years of Dr. William H. Luedde, St. Louis, to the American Committee (Joint) on Optics and Visual Physiology.

Reelection for four years of Dr. S. Judd Beach, Portland, Maine, to the American Board of Ophthalmology.

To the Committee of National Museum of Ophthalmic (Joint) Pathology, Dr. Jonas S. Friedenwald, Baltimore.

Reelection of Dr. Georgiana Dvorak Theobald, Oak Park, Ill., to fill the vacancy of chairman of the Committee for Scientific Exhibit from the Section. The appointment of Dr. Derrick Vail, Cincinnati, and Dr. John E. L. Keyes, Youngstown, Ohio, to the committee.

The election of Dr. Robert Von der Heydt, Chicago, Dr. Burton Chance, Philadelphia, Dr. J. W. Jervey, Greenville, S. C., and Dr. Hans Barkan, San Francisco, to constitute the Committee on Museum of Ophthalmic History.

Election for three years of Dr. Maynard C. Wheeler, New York, to fill a vacancy on the American Council on Orthoptics.

To the Advisory Committee of Student Health Association, the reelection of Dr. William L. Benedict, Rochester, Minn.

To discontinue the committee from the Section to Cooperate with the National Committee for the Prevention of Blindness.

To continue for one year the present Committee on Ophthalmic Literature (Joint).

The election of Dr. Alfred Cowan, Philadelphia, to the Committee on Visual Economics.

Scientific Session

Dr. Alan C. Woods, Baltimore, read a paper on "The Effect of Sensitivity and Immunity on the Experimental Lesions of Ocular Tuberculosis." Discussed by Drs. Edwin W. Burton, Charlottesville, Va.; Merrill J. King, Boston, and Alan C. Woods, Baltimore.

Dr. Alson E. Braley, Detroit, read a paper on "Intracellular Bodies of the Conjunctival Epithelial Cells." Discussed by Drs. Phillips Thygeson, New York, and Alson E. Braley, Detroit.

Dr. Albert E. Sloane, Boston, read a paper on "Massachusetts Vision Test: An Improved Method of School Eye Testing." Discussed by Drs. S. Judd Beach, Portland, Maine; Maynard C. Wheeler, New York; S. Weir Newmayer, Philadelphia; Edward Jackson, Denver, and Albert E. Sloane, Boston.

Demonstration Session

Dr. Dikran M. Yazujian, Trenton, N. J., presented an apparatus for localizing intra-ocular foreign bodies.

Dr. Albert E. Sloane, Boston, presented experimental apparatus for the Massachusetts vision test.

Dr. Walter B. Lancaster, Boston, demonstrated some magnets.

Dr. Conrad Berens, New York, presented muscle forceps without teeth; a curved glaucoma knife; a cataract knife.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Nervous and Mental Diseases.

Executive Session

Dr. Arthur J. Bedell, Albany, N. Y., reported as delegate to the House of Delegates that the resolution of the section was unanimously adopted by the House of Delegates.

Dr. Henry R. Viets, Boston, reported as delegate to the House of Delegates from the Section on Nervous and Mental Diseases that the resolution dealing with the endorsement of the Central Neuro-Psychiatric Institute as proposed by the United States Public Health Service failed of passage in the House; that the resolution dealing with the so-called Pennsylvania Plan of training in legal psychiatry was tabled. Dr. Viets

suggested that the section itself have a committee to consider resolutions, and that the resolutions be put in the first day of the meeting and referred to a committee of the section.

Scientific Session

Dr. Walter E. Dandy, Baltimore, read a paper on "Results Following the Intracranial Approach for Orbital Tumors." Discussed by Drs. Arnold Knapp, New York; William L. Benedict, Rochester, Minn., and Walter E. Dandy, Baltimore.

Drs. Ward C. Halstead and A. Earl Walker, Chicago, presented a paper on "Sparing and Nonsparing of 'Macular' Vision Associated with Occipital Lobectomy in Man." Discussed by Drs. Wilder G. Penfield, Montreal; P. J. Leinfelder, Iowa City; Tracy J. Putnam, New York; W. Ivan Lillie, Philadelphia, and A. Earl Walker, Chicago.

Dr. Albert D. Ruedemann, Cleveland, read a paper on "Comparison of Differential Diagnosis of Brain Lesions by Visual Fields, Encephalography and Ventriculography." Discussed by Drs. John N. Evans, Brooklyn, and Albert D. Ruedemann, Cleveland.

Dr. Francis H. Adler, Philadelphia, read a paper on "Primary Pituitary Adenomas and the Syndrome of the Cavernous Sinus." Discussed by Drs. William J. German Jr., New Haven, Conn.; Oscar Hirsch, Boston, and Francis H. Adler, Philadelphia.

Dr. W. Ivan Lillie, Philadelphia, read a paper on "Prechiasmal Syndrome Produced by Chronic Local Arachnoiditis." Discussed by Drs. Temple S. Fay, Philadelphia; Derrick Vail, Cincinnati, and W. Ivan Lillie, Philadelphia.

Drs. Robert B. Aird and Howard C. Naffziger, San Francisco, read a paper on "The Myopathy and Etiology of Exophthalmos Experimentally Produced by Extracts of the Anterior Pituitary." Discussed by Drs. David Marine, New York; Harry B. Friedgood, Boston; Derrick Vail, Cincinnati, and Robert B. Aird, San Francisco.

SECTION ON LARYNGOLOGY, OTOTOLOGY AND RHINOLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Arthur W. Proetz, St. Louis.

Dr. Leon Felderman, Philadelphia, read a paper on "Ethmosphenoidal Epiglottidean Syndrome Interfering with Vocal Range." Discussed by Drs. James S. Greene, New York; Irving W. Voorhees, New York, and Leon Felderman, Philadelphia.

Dr. Mercer G. Lynch, New Orleans, read a paper on "Geographic Virulence of Mastoiditis." Discussed by Drs. Noah D. Fabricant, Chicago; Lester A. Brown, Atlanta, Ga., and Mercer G. Lynch, New Orleans.

Dr. Frederick T. Hill, Waterville, Maine, read a paper on "Diagnostic Pitfalls in the Nasopharynx."

Dr. Frederick A. Figi, Rochester, Minn., read a paper on "Fibromas of the Nasopharynx."

These two papers were discussed by Drs. Joseph D. Kelly, New York; Charles J. Imperatori, New York; Gordon B. New, Rochester, Minn.; Frederick T. Hill, Waterville, Maine, and Frederick A. Figi, Rochester, Minn.

Dr. Harold A. Fletcher, San Francisco, read a paper on "Industrial Aspects of Ear, Nose and Throat Practice." Discussed by Drs. W. E. Grove, Milwaukee; H. A. Kuhn, Hammond, Ind.; Walter F. Schaller, San Francisco; Rea E. Ashley, San Francisco, and Harold A. Fletcher, San Francisco.

Dr. W. Likely Simpson, Memphis, Tenn., read a paper on "Osteoma of the Mastoid Process." Discussed by Dr. George M. Coates, Philadelphia.

THURSDAY, JUNE 13—AFTERNOON

Executive Session

The following officers were elected: chairman, Dr. LeRoy A. Schall, Boston; vice chairman, Dr. W. E. Grove, Milwaukee; secretary, Dr. Louis H. Clerf, Philadelphia; executive committee: Dr. H. Marshall Taylor, Jacksonville, Fla.; Dr. Arthur W. Proetz, St. Louis, and Dr. LeRoy A. Schall, Boston; delegate, Dr. Burt R. Shurly, Detroit; alternate, Dr. Gordon F. Harkness, Davenport, Iowa.

Dr. H. Marshall Taylor, Jacksonville, Fla., reported that the Committee on Swimming had no report to make and asked that the committee be discharged. On motion, duly seconded and carried, the committee was discharged, with thanks.

Scientific Session

Dr. Arthur W. Proetz, St. Louis, read the chairman's address, entitled "The Functional Point of View in Rhinology."

Dr. J. MacKenzie Brown, Los Angeles, read a paper on "The Treatment of Acute and Chronic Sinus Disease."

Dr. Harold I. Lillie, Rochester, Minn., read a paper on "The Treatment of Acute and Chronic Otitis Media."

Dr. Lyman G. Richards, Boston, read a paper on "The Treatment of Diseases of the Throat."

An open forum with questions from the floor was held on these three papers.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Radiology. The proceedings are reported in the minutes of that section.

SECTION ON PEDIATRICS

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:10 by the chairman, Dr. Albert D. Kaiser, Rochester, N. Y.

Dr. F. M. Pottenger Jr., Monrovia, Calif., read a paper on "The Role of Nutrition in the Production of Childhood Asthma." Discussed by Drs. W. Ambrose McGee, Richmond, Va., and F. M. Pottenger Jr., Monrovia, Calif.

Dr. Frank Lee Bivings, Atlanta, Ga., read a paper on "Asthmatic Bronchitis Following Chronic Upper Respiratory Infection." Discussed by Drs. Hal M. Davison, Atlanta, Ga.; Warren W. Quillian, Coral Gables, Fla.; Harry Lowenburg Jr., Philadelphia, and Frank Lee Bivings, Atlanta, Ga.

A committee on resolutions was appointed by the chairman, composed of Drs. John Aikman, Rochester, N. Y.; Victor J. Greenbaum, Cincinnati, and Gilbert J. Levy, Memphis, Tenn.

Drs. Clifford D. Sweet, Lawrence R. Jacobus and Henry E. Stafford, Oakland, Calif., presented a paper on "Child-Parent Relationships." Discussed by Drs. Oscar Reiss, Los Angeles; I. Edward Liss, New York, and Clifford D. Sweet, Oakland, Calif.

Drs. F. W. Schlutz and Elizabeth M. Knott, Chicago, presented a paper on "Factors Which Affect the Level of Vitamin B₁ in the Blood of Infants and Children." Discussed by Dr. Herbert Pollack, New York.

Dr. Lee Forrest Hill, Des Moines, Iowa, read a paper on "Scope of the Health Examination for Well Children," which was followed by a talking picture, "Bobby Goes to School."

THURSDAY, JUNE 13—MORNING

Dr. John Aikman, Rochester, N. Y., chairman of the resolutions committee (which also serves as the executive committee), presented the following resolutions, which, on motion regularly made and seconded, it was voted to approve:

Resolved, That in the death of Dr. John Lovett Morse the Section on Pediatrics of the American Medical Association and the pediatric profession of the United States have lost an outstanding pioneer, leader and teacher. Dr. Morse at all times gave freely of himself to the advancement of pediatrics and has left an indelible influence on pediatrics in America. His loyalty and his contributions to this section have been invaluable.

Resolved, That this motion be placed in the minutes of the Section on Pediatrics and that a copy be sent to the family of Dr. Morse.

Resolved, That the Section on Pediatrics extends thanks and appreciation to Dr. Adolf De Sanctis and his committee for the generous hospitality and many courtesies shown to the section during this meeting.

The committee also moved that a telegram be sent to Dr. Edward Clay Mitchell, Memphis, Tenn., member of the executive committee, expressing disappointment in his absence during the meeting and wishing him a speedy recovery from his illness. This motion was seconded, put to a vote and carried.

The chairman called attention to the fact that an index to the AMERICAN JOURNAL OF DISEASES OF CHILDREN was dependent on the number of demands for such an index and urged that

members desiring the index communicate with Dr. Clifford G. Grulee, Evanston, Ill., who was in charge of this work.

The following officers were elected: chairman, Dr. Julius H. Hess, Chicago; vice chairman, Dr. John A. Toomey, Cleveland; secretary, Dr. Hugh L. Dwyer, Kansas City, Mo.; delegate, Dr. William Weston, Columbia, S. C.; alternate, Dr. A. Graeme Mitchell, Cincinnati; executive committee: Dr. John Aikman, Rochester, N. Y.; Dr. J. Victor Greenbaum, Cincinnati, and Dr. Gilbert J. Levy, Memphis, Tenn.; representative in charge of the scientific section, Dr. Arthur F. Abt, Chicago.

The chairman reported for the Abraham Jacobi Fund in the absence of the secretary, stating that \$22.53 had been added to the fund during the year; also on June 12 a payment of \$481 had been authorized to cover the landscaping and planting of the grounds around Dr. Jacobi's grave in Bolton Landing, N. Y., and a further amount, not to exceed \$75, for the maintenance of the grounds each year; also that the sum of \$1,500 which had been authorized for the fifth International Congress of Pediatrics which was to have been held in Boston in 1940 and which meeting had been indefinitely postponed, was to be restored to the fund until such time as such a meeting could be held.

The chairman also reported the suggestion of the secretary that each year some one be invited to address the Section on Pediatrics as an Abraham Jacobi lecturer, the amount of money to be spent on this as an honorarium to the lecturer not to exceed \$100. The amount in the Abraham Jacobi Fund at the present time amounted to \$7,500.

Dr. Albert D. Kaiser, Rochester, N. Y., read the chairman's address, entitled "Significance of the Tonsils in the Development of the Child."

The following papers were read in a Panel Discussion on Some Contagious Diseases, during which Dr. John A. Toomey, Cleveland, presided:

Erling S. Platou, Minneapolis: "Convalescent Serums."

Dr. Gladys Henry Dick, Chicago: "Scarlet Fever: Active and Passive Immunity."

Dr. Conrad Wesselhoeft, Boston: "Nephritis in Scarlet Fever and Its Treatment."

Dr. Charles F. McKhann, Boston: "Measles Prevention."

Dr. Archibald L. Hoyne, Chicago: "Treatment of Epidemic Meningitis."

Dr. Louis W. Sauer, Evanston, Ill.: "Active Immunity in Whooping Cough."

Dr. Joseph Stokes Jr., Philadelphia: "Epidemic Influenza: Diagnosis."

Dr. John A. Toomey, Cleveland: "Differential Diagnosis of Various Forms of Encephalitis."

Following the presentation of these papers, questions were submitted by the members of the section and answered by the particular member of the panel to whom they were directed.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Obstetrics and Gynecology.

Dr. Priscilla White, Boston, read a paper on "Prediction and Prevention of Pregnancy Accidents in Diabetes."

Dr. Warren R. Sisson, Boston, read a paper on "The Neonatal Problem in Infants of Diabetic Mothers."

These two papers were discussed by Drs. J. A. Lamphier, Brooklyn, and Priscilla White, Boston.

Dr. Edith L. Potter, Chicago, read a paper on "A Study of Fetal and Neonatal Deaths: A Statistical Review." Discussed by Drs. Ludwig A. Emge, San Francisco, and Edith L. Potter, Chicago.

Drs. Ethel C. Dunham and Jessie M. Bierman, Washington, D. C., presented a paper on "The Care of the Premature Infant." Discussed by Drs. Harry Lowenburg, Philadelphia, and Ethel C. Dunham, Washington, D. C.

Dr. Julius H. Hess, Chicago, read a paper on "The Responsibilities of the Newborn Service from the Standpoint of the Pediatrician."

Dr. W. W. Waddell Jr., Charlottesville, Va., read a paper on "Vitamin K in the Prevention and Treatment of Prothrombin

Deficiency and Associated Hemorrhage in the Newborn." Discussed by Drs. Clifford D. Sweet, Oakland, Calif.; Chester R. Brown, Arlington, N. J., and W. W. Waddell Jr., Charlottesville, Va.

SECTION ON PHARMACOLOGY AND THERAPEUTICS

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:05 by the chairman, Dr. Irving S. Wright, New York.

Drs. Verne W. Swigert, Evanston, Ill., and Reginald Fitz, Boston, presented a paper on "The Effect of Mersalyl (Salyrgan) on Plasma and Blood Volume." Discussed by Drs. Leonard G. Rowntree, Philadelphia; Maurice Bruger, New York; George R. Herrmann, Galveston, Texas., and Verne W. Swigert, Evanston, Ill.

Drs. Meyer Bodansky, J. L. Jenkins, H. Levine and A. J. Gilbert, Galveston, Texas, presented a paper on "Clinical and Experimental Studies on Paraldehyde." Discussed by Drs. S. Bernard Wortis, New York; Norman H. Jolliffe, New York; Reginald Fitz, Boston, and Meyer Bodansky, Galveston, Texas.

Dr. M. I. Smith, Washington, D. C., read a paper entitled "A Review of the More Recent Field and Laboratory Studies in Chronic Selenium Poisoning." Discussed by Dr. J. H. Sterner, Rochester, N. Y.

Drs. Bernard M. Jacobson and Yellapragada Subbarow, Boston, presented a paper on "Studies of the Principle in Liver Effective in Pernicious Anemia: VI. Recent Advances in the Purification of Active Substances." Discussed by Drs. Randolph West, New York; W. T. Salter, Boston, and Bernard M. Jacobson, Boston.

Drs. Charles Mazer, S. Leon Israel and Elkin Ravetz, Philadelphia, presented a paper on "An Experimental and Clinical Evaluation of the Synthetic Estrogen Stilbestrol." Discussed by Drs. Theodore Neustaedter, New York; L. M. Randall, Rochester, Minn.; A. A. Herold, Shreveport, La., and Charles Mazer, Philadelphia.

Drs. Joseph B. Kirsner and Walter L. Palmer, Chicago, presented a paper on "The Role of Chlorides in the Treatment of Alkalosis." Discussed by Drs. Dana W. Atchley, New York; L. C. Gatewood, Chicago; E. N. Collins, Cleveland, and Joseph B. Kirsner, Chicago.

THURSDAY, JUNE 13—MORNING

The chairman reported to the section the recommendation of the executive committee that the name of the section be changed to Section on Therapeutics and Experimental Medicine. On the motion of Dr. Joseph B. Wolfe, Philadelphia, it was unanimously voted that this change be recommended to the House of Delegates.

The following officers were elected: chairman, Dr. C. M. Gruber, Philadelphia; vice chairman, Dr. Wallace M. Yater, Washington, D. C.; secretary, Dr. Edgar V. Allen, Rochester, Minn.; delegate, Dr. Irving S. Wright, New York; alternate, Dr. O. P. J. Falk, St. Louis; executive committee: Drs. Erwin E. Nelson, New Orleans; Irving S. Wright, New York, and C. M. Gruber, Philadelphia.

Dr. Irving S. Wright, New York, read the chairman's address, entitled "Social Significance and Ultimate Objective of the Treatment of Arteriosclerosis Obliterans."

Drs. James G. Carr, Alexander Sanders and Gilbert H. Marquardt, Chicago, presented a paper on "The Treatment of Angina Pectoris by Pancreatic Tissue Extract." Discussed by Drs. A. Wilbur Duryce, New York; Emanuel Libman, New York; T. K. Lewis, Birmingham, Ala.; Joseph B. Wolfe, Philadelphia; Anna Samuelson, New York; John F. Casey, Boston, and Gilbert H. Marquardt, Chicago.

Dr. Jerome W. Conn, Ann Arbor, Mich., read a paper on "The Spontaneous Hypoglycemia: The Importance of Etiology in Determining Treatment." Discussed by Drs. Herbert Pollack, New York; E. J. Kepler, Rochester, Minn.; G. M. Churukian, Paris, Ill., and Jerome W. Conn, Ann Arbor, Mich.

Dr. A. R. MacLean, Rochester, Minn., read a paper on "The Treatment of Orthostatic Hypotension and Orthostatic Tachy-

cardia." Discussed by Drs. Horace Korn, Iowa City; O. P. J. Falk, St. Louis, and A. R. MacLean, Rochester, Minn.

Dr. William P. Murphy, Boston, read a paper entitled "A Note of Optimism in the Treatment of the Patient with Chronic Leukemia." Discussed by Drs. Irving S. Wright, New York; H. J. Ullmann, Santa Barbara, Calif.; Paul Reznikoff, New York; Claude E. Forkner, New York, and William P. Murphy, Boston.

Drs. E. N. Collins, Cleveland, C. P. Pritchett, Columbus, Ohio, and H. R. Rossmiller, Cleveland, presented a paper on "The Use of Aluminum Hydroxide in the Treatment of Peptic Ulcer." Discussed by Drs. James Flexner, New York; Arthur J. Atkinson, Chicago; I. H. Einsel, Cleveland; Manfred Kraemer, Newark, N. J.; Isidor Greenwald, New York, and E. N. Collins, Cleveland.

Drs. Harrison F. Flippin, Leon Schwartz and John G. Reinhold, Philadelphia, presented a paper on "Sulfathiazole and Sulfapyridine Therapy in Pneumonia." Discussed by Drs. Herbert K. Ensworth, New York; Elmer H. Loughlin, Brooklyn; John F. Casey, Boston, and Harrison F. Flippin, Philadelphia.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Practice of Medicine.

Drs. Francis D. Murphy, Milwaukee, Howard L. Correll, Wauwatosa, Wis., and John C. Grill, Milwaukee, presented a paper on "The Effects of Intravenous Solutions on Patients With and Without Cardiovascular Defects." Discussed by Drs. N. C. Gilbert, Chicago, and Irvine H. Page, Indianapolis.

Drs. Arthur Grollman, Baltimore, and J. R. Williams Jr. and T. R. Harrison, Nashville, Tenn., presented a paper on "The Antipressor Action of Renal Extracts." Discussed by Drs. J. Murray Steele, New York; M. C. Winternitz, New Haven, Conn.; Edgar V. Allen, Rochester, Minn.; Frederick M. Allen, New York; Benjamin Jablons, New York, and T. R. Harrison, Nashville, Tenn.

Dr. Paul Padgett, Baltimore, read a paper on "Long-Term Results in the Treatment of Early Syphilis." Discussed by Dr. Joseph Earle Moore, Baltimore.

Drs. Wallace E. Herrell and Alex E. Brown, Rochester, Minn., presented a paper on "The Treatment of Septicemia: Results Before and Since the Advent of Sulfamido Compounds." Discussed by Drs. Perrin H. Long, Baltimore, and Wallace E. Herrell, Rochester, Minn.

SECTION ON PATHOLOGY AND PHYSIOLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2:05 by the chairman, Dr. Frank W. Hartman, Detroit.

The following papers were read as a symposium on "Anoxia": Dr. Ernst Gellhorn, Chicago: "Fundamental Principles in the Adjustment Reactions of the Organisms to Anoxia."

Dr. Carl J. Wiggers, Cleveland: "Cardiac Adaptations During Anoxia."

Dr. H. E. Himwich, Albany, N. Y.: "Anoxia and the Treatment of Schizophrenia."

Dr. Ralph M. Waters, Madison, Wis.: "Anoxia from the Anesthetist's Point of View."

Dr. Nicholson J. Eastman, Baltimore: "A Study of Alpha-Lobeline, Metrazol and Nikethamide in Experimental Anoxia."

Dr. Frank W. Hartman, Detroit: "Pathology in Anoxia," the chairman's address.

These six papers were discussed by Drs. F. A. D. Alexander, Albany, N. Y.; Robert L. Levy, New York; R. D. McClure, Detroit; Ernst Gellhorn, Chicago; Carl J. Wiggers, Cleveland; Harold Inman Gosline, Ossining, N. Y.; H. E. Himwich, Albany, N. Y.; Ralph M. Waters, Madison, Wis.; Frank W. Hartman, Detroit; Alvin G. Foord, Pasadena, Calif., and Nicholson J. Eastman, Baltimore.

Dr. L. W. Larson, Bismarck, N. D., delegate of the section to the House of Delegates, submitted his report, dealing principally with the expansion of state public health laboratory

work. Dr. Larson also reported on efforts being made to change the name of the section to "Section on Experimental Medicine" and offered the following resolution, which was unanimously adopted:

WHEREAS, The suggestion has been made to the Council on Scientific Assembly of the American Medical Association that the Section on Pathology and Physiology be combined with the Section on Pharmacology and Therapeutics to form a Section on Experimental Medicine; be it

Resolved, That the Section on Pathology and Physiology is opposed to such a change.

Drs. Frank W. Hartman, Detroit, and J. J. Moore, Chicago, were nominated for six year terms on the American Board of Pathology.

THURSDAY, JUNE 13—AFTERNOON

Dr. James F. Rinehart, San Francisco, read a paper on "Capillary Strength and Permeability in Rheumatoid Arthritis."

Dr. Max Cutler, Chicago, read a paper on "Cancer of the Larynx: Relation Between Gross Anatomy, Microscopic Structure and Radiosensitivity." Discussed by Drs. Chevalier L. Jackson, Philadelphia; Frank W. Konzelmann, Philadelphia, and Max Cutler, Chicago.

Dr. M. C. Winternitz, New Haven, Conn., read a paper on "Effects of Tissue Extracts on Normal and Nephrectomized Dogs." Discussed by Dr. Benjamin Jablons, New York.

Drs. Don C. Sutton and John Ashworth, Chicago, presented a paper on "Experimental Lesions of the Aorta Simulating Arteriosclerosis." Discussed by Drs. K. K. Jones, Chicago; J. P. Simonds, Chicago; M. C. Winternitz, New Haven, Conn., and Don C. Sutton, Chicago.

Dr. H. E. Robertson, Rochester, Minn., read a paper on "The Pathology of Brunner's Glands." Discussed by Dr. Carl J. Wiggers, Cleveland.

Drs. Ernest W. Page, Berkeley, Calif.; Henry S. Patton, Oakland, Calif., and Eric Ogden, Berkeley, Calif., presented a paper on "The Effect of Pregnancy on Experimental Hypertension." Discussed by Drs. Irvine H. Page, Indianapolis; Hans Selye, Montreal, Canada; Frank W. Hartman, Detroit; L. V. Dill, New York; T. R. Harrison, Nashville, Tenn., and Eric Ogden, Berkeley, Calif.

Dr. Hans Selye, Montreal, read a paper on "Compensatory Atrophy of Endocrine Glands." Discussed by Drs. Milton Steinberg, Chicago; J. P. Simonds, Chicago, and Hans Selye, Montreal.

A nominating committee was appointed, consisting of Drs. L. W. Larson, Bismarck, N. D.; H. C. Thornton, Indianapolis, and Alvin Foord, Pasadena, Calif.

FRIDAY, JUNE 14—AFTERNOON

The following officers were elected: chairman, Dr. Carl J. Wiggers, Cleveland; vice chairman, Dr. J. P. Simonds, Chicago; secretary, Dr. J. J. Moore, Chicago; delegate, Dr. L. W. Larson, Bismarck, N. D.; alternate, Dr. J. J. Moore, Chicago; executive committee: Drs. M. B. Visscher, Minneapolis; Frank W. Hartman, Detroit, and Carl J. Wiggers, Cleveland.

Drs. H. J. Corper, A. P. Damerow and Maurice L. Cohn, Denver, presented a paper on "Tuberculinprotein Desensitization and Tuberculosis." Discussed by Dr. Henry C. Sweany, Chicago.

Drs. G. B. Fantley, A. C. Ivy and A. J. Atkinson, Chicago, presented a paper on "The Use of Aluminum Phosphate in the Therapy of Peptic Ulcer." Discussed by Drs. Jesse L. Bollman, Rochester, Minn.; Hyman I. Goldstein, Camden, N. J.; I. H. Einsel, Cleveland, and A. C. Ivy, Chicago.

Drs. Elmer L. De Gowin and Robert C. Hardin, Iowa City, presented a paper on "Studies on Preserved Human Blood: VI. Reactions from Transfusion." Discussed by Drs. Alexander S. Wiener, Brooklyn; L. W. Diggs, Memphis, Tenn.; Hyman I. Goldstein, Camden, N. J.; Alvin G. Foord, Pasadena, Calif., and Elmer L. De Gowin, Iowa City.

Drs. Sidney O. Levinson, Frank E. Rubovits Jr. and Heinrich Necheles, Chicago, presented a paper on "Human Serum Transfusions." Discussed by Drs. Joseph A. Wagner, Bryn Mawr, Pa., and Sidney O. Levinson, Chicago.

Dr. Jesse L. Bollman, Rochester, Minn., read a paper on "The Influence of the Liver on the Utilization of Vitamin K."

Discussed by Drs. Stephen J. Maddock, Boston; Jonathan Rhoads, Philadelphia, and Jesse L. Bollman, Rochester, Minn.

Drs. Henry C. Sweany and Charlotte Louise Clancy, Chicago, and Molly H. Radford, Santa Fe, N. M., presented a paper on "The Body Economy of Vitamin C in Health and Disease with Special Studies in Tuberculosis."

Dr. Bernhard Steinberg, Toledo, Ohio, read a paper on "Peritoneal Exudate: A Guide for the Diagnosis and Prognosis of Peritoneal Conditions." Discussed by Drs. Frank L. Meloney, New York, and Bernhard Steinberg, Toledo, Ohio.

SECTION ON NERVOUS AND MENTAL DISEASES

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:25 by the chairman, Dr. Paul C. Bucy, Chicago.

Drs. William F. Petersen, Chicago, and Hans H. Reese, Madison, Wis., presented a paper on "Psychotic and Somatic Interrelations." Discussed by Lloyd H. Ziegler, Wauwatosa, Wis.; Irving J. Sands, Brooklyn, and Hans H. Reese, Madison, Wis.

Dr. A. R. Vonderahe, Cincinnati, read a paper on "Sequelae of Severe Disease of the Abdominal Viscera with Special Reference to Psychoneurosis and Imbalance of the Autonomic Nervous System." Discussed by Drs. Leo Alexander, Boston; Robert G. Green, Minneapolis; Norman Jolliffe, New York; John F. Fulton, New Haven, Conn., and A. R. Vonderahe, Cincinnati.

Dr. Samuel D. Ingham, Los Angeles, read a paper on "Instinctive Motivations of Suicide." Discussed by Drs. A. A. Brill, New York; Titus H. Harris, Galveston, Texas, and Samuel D. Ingham, Los Angeles.

Drs. Herbert Jasper, John Kershman and A. R. Elvidge, Montreal, presented a paper on "Electro-Encephalographic Studies of Head Injury." Discussed by Drs. Tracy J. Putnam, New York; Robert S. Schwab, Boston; Max H. Weinberg, Pittsburgh, and John Kershman, Montreal.

Dr. Russell N. DeJong, Ann Arbor, Mich., read a paper on "Acute Ascending Paralysis with Clinical and Pathologic Report on Cases with Fatal Termination."

Drs. Paul H. Garvey, Nathaniel Jones and Stafford L. Warren, Rochester, N. Y., presented a paper on "Polyradiculoneuritis (Guillain-Barré Syndrome)."

These two papers were discussed by Drs. Louis Casamajor, New York; Peter Bassoc, Chicago; A. M. Ornstein, Philadelphia; Frederick P. Moersch, Rochester, Minn.; A. E. Bennett, Omaha; Norman Jolliffe, New York; Paul C. Bucy, Chicago; Irving J. Sands, Brooklyn; A. M. Rabiner, Brooklyn; Ralph Hayward, Toronto; Russell N. DeJong, Ann Arbor, Mich., and Paul H. Garvey, Rochester, N. Y.

THURSDAY, JUNE 13—MORNING

The following officers were elected: chairman, Tom B. Throckmorton, Des Moines, Iowa; vice chairman, Titus H. Harris, Galveston, Texas; secretary, Johannes M. Nielsen, Los Angeles; executive committee: Francis C. Grant, Philadelphia; Paul C. Bucy, Chicago, and Tom B. Throckmorton, Des Moines, Iowa; delegate, Henry R. Viets, Boston; alternate, R. P. Mackay, Chicago; representative to Scientific Exhibit, Frederick P. Moersch, Rochester, Minn.; representative on American Board of Psychiatry and Neurology, Lloyd H. Ziegler, Wauwatosa, Wis.; representative on American Board of Neurosurgery, Paul C. Bucy, Chicago.

Dr. Walter Freeman, Washington, D. C., gave a report from the American Board of Psychiatry and Neurology, which was accepted.

Dr. Paul C. Bucy, Chicago, gave a report from the American Board of Neurosurgery, which was accepted.

The section approved for transmittal to the House of Delegates a resolution recommending the establishment in the United States Public Health Service of an institute for the study of mental and nervous diseases.

The section approved for transmittal to the House of Delegates a resolution approving the plan known as the Pennsylvania plan applicable to medicolegal cases in the handling of criminals.

Dr. Frederick P. Moersch, Rochester, Minn., read a paper on "Primary and Secondary Melanoma of the Central Nervous System." Discussed by Drs. S. Bernard Wortis, New York; Peter Bassoe, Chicago; Hans H. Reese, Madison, Wis., and Frederick P. Moersch, Rochester, Minn.

Drs. Bernard J. Alpers and F. H. Lewy, Philadelphia, presented a paper on "The Nervous System in Carbon Disulfide Poisoning in Animals and Man." Discussed by Drs. S. T. Gordy, Philadelphia; Armando Ferraro, New York; Philip Drinker, Cambridge, Mass.; Noble R. Chambers, Syracuse, N. Y.; Bernard J. Alpers, Philadelphia, and F. H. Lewy, Philadelphia.

Dr. Paul C. Bucy, Chicago, read the chairman's address, entitled "Surgical Neurology and Biology."

Drs. Louis J. Karnosh, Cleveland, and Roger F. Scherb, Camarillo, Calif., presented a paper on "The Significance of Trophic Lesions in the Trigeminal Area." Discussed by Drs. Max Minor Peet, Ann Arbor, Mich.; A. Earl Walker, Chicago, and Byron Stookey, New York.

Drs. Orthello R. Langworthy and Frederick H. Hesser, Baltimore, presented a paper on "The Control of Smooth Muscle by the Nervous System." Discussed by Drs. J. W. Watts, Washington, D. C.; Lloyd G. Lewis, Baltimore, and John F. Fulton, New Haven, Conn.

Drs. Eric Oldberg and W. A. Gustafson, Chicago, presented a paper on "The Neurologic Significance of Platybasia." Discussed by Drs. Tracy J. Putnam, New York; Leo M. Davidoff, Brooklyn, and Eric Oldberg, Chicago.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Ophthalmology. The proceedings are reported in the minutes of that section.

SECTION ON DERMATOLOGY AND SYPHILOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:15 by the chairman, Dr. John G. Downing, Boston.

Dr. John G. Downing read the chairman's address, entitled "Dermatitis."

Drs. James W. Jordan and Earl D. Osborne, Buffalo, presented a paper on "Dermatitis of the Hands in Housewives: Role of Soaps in Its Etiology and Methods for Its Prevention." Discussed by Drs. Joseph V. Klauder, Philadelphia; Marion B. Sulzberger, New York; Herman Goodman, New York; Joseph Muller, Worcester, Mass.; Adolph Rostenberg Jr., Washington, D. C.; Howard J. Parkhurst, Toledo, Ohio; Donald M. Pillsbury, Philadelphia, and James W. Jordan, Buffalo.

Dr. John H. Stokes, Philadelphia, read a paper on "The Personality Factor in the Psychoneurogenous Reactions of the Skin." Discussed by Drs. Harry C. Solomon, Boston; Eugene T. Bernstein, New York; Henry D. Niles, New York; S. William Becker, Chicago; Samuel Ayres Jr., Los Angeles; Joseph V. Klauder, Philadelphia; Marion B. Sulzberger, New York, and John H. Stokes, Philadelphia.

Dr. Lawrence C. Goldberg, Cincinnati, read a paper on "Histaminase (Torantil) in the Treatment of Allergic Dermatoses." Discussed by Drs. G. Marshall Crawford, Boston; Ashton L. Welsh, Cincinnati; Herman Goodman, New York; Herman Sharlii, New York, and Lawrence C. Goldberg, Cincinnati.

Dr. M. H. Goodman, Baltimore, read a paper on "Dermatitis Herpetiformis: Influence of Age Factors and a Study of Pathologic Data with Special Reference to Eosinophils." Discussed by Drs. Isadore Rosen, New York; Jacob H. Swartz, Boston; Henry D. Niles, New York; Theodore Cornbleet, Chicago, and M. H. Goodman, Baltimore.

Dr. Stephen Epstein, Marshfield, Wis., read a paper on "Staphylococcal Impetigo Contagiosa." Discussed by Drs. Marion B. Sulzberger, New York; Richard S. Weiss, St. Louis, and Stephen Epstein, Marshfield, Wis.

Dr. John F. Madden, St. Paul, read a paper on "Treatment of Psoriasis." Discussed (at the Thursday session) by Drs. Donald M. Pillsbury, Philadelphia; Joseph V. Klauder, Philadelphia, and John F. Madden, St. Paul.

THURSDAY, JUNE 13—MORNING

The chairman asked that any member having business to go before the House of Delegates should present it on the floor during this business session.

The chairman then introduced Dr. Jose J. Puento, Buenos Aires.

It was moved by Dr. Harold N. Cole, Cleveland, seconded by Dr. Paul A. O'Leary, Rochester, Minn., and carried, that Dr. Puento be given the courtesy of the floor.

Dr. Hamilton Montgomery, Rochester, Minn., representative to the Scientific Exhibit from the section, read his prepared report. (Paper No. 1.)

The Chairman appointed the following auditing committee to audit Dr. Montgomery's financial statement: Drs. William P. Boardman, Boston; W. M. Sams, Miami, Fla., and H. F. Anderson, Washington, D. C.

Dr. Paul A. O'Leary, Rochester, Minn., turned in the financial report on the International Congress of Dermatology and Syphilology. He stated that the expenditures had been about \$2,000 and that there was a balance of a few hundred dollars on hand which they did not know what to do with but were appreciative of the financial efforts of those who contributed to the fund and were sorry that the balance had not been put to better use.

Dr. C. Guy Lane, Boston, gave his report of the American Board of Dermatology and Syphilology.

Reporting for the Committee on Industrial Dermatoses, Dr. C. Guy Lane, Boston, stated: The committee has agreed on a definition and is working out the criteria of occupational dermatoses, with a view of submitting these criteria to the Council on Industrial Health of the American Medical Association. A list of primary irritants is also being prepared by the committee, and there is also a study of the so-called eczematous substances. There has been, and there will be again today, a discussion with members of the Council on Industrial Health on the matter of setting up a central clearing house, perhaps, for a further study of occupational dermatoses, possibly with reference to the collection of reports with reference to the application of criteria regarding reportability of data, of reference material, and so on, and a further report on these items will be rendered next year.

It was moved by Dr. C. Guy Lane, Boston, seconded by Dr. Francis P. McCarthy, Boston, and carried, that in view of the fact that a committee was appointed at the American Dermatological Association for a further study of contact dermatoses, a similar committee of three be appointed by the chairman to cooperate with the committee from the American Dermatological Association, and also probably a committee from the investigative society, to continue to cooperate in such investigations.

The auditing committee appointed to audit the report on the Scientific Exhibit reported that it approved the report.

Dr. Francis P. McCarthy, Boston, read a paper on "A Clinical and Pathologic Study of Oral Disease, Based on 2,300 Consecutive Cases." Discussed by Drs. Frank J. Eichenlaub, Washington, D. C.; Samuel Ayers Jr., Los Angeles, and Francis P. McCarthy, Boston.

Drs. William H. Guy, Bernhard A. Goldmann, George P. Gannon and Jacob Slone, Pittsburgh, presented a paper on "Acetylglyco-Arsenobenzene in the Treatment of Syphilis." Discussed by Drs. Harry M. Robinson, Baltimore; Joseph Earle Moore, Baltimore, and William H. Guy, Pittsburgh.

Drs. Harold N. Cole, Gerard A. DeOreo, James R. Driver and Herbert H. Johnson Jr., Cleveland, and Walter F. Schwartz, Pasadena, Calif., presented a paper on "The Use of Bismuth Injections to Control the Course of Therapeutic Malaria." Discussed by Drs. Paul A. O'Leary, Rochester, Minn., and Harold N. Cole, Cleveland.

Dr. Edmund N. Walsh, Chicago, read a paper on "The Use of Bismuth in Syphilotherapy." Discussed by Drs. Donald M. Pillsbury, Philadelphia, and S. William Becker, Chicago.

Dr. Albert Strickler, Philadelphia, read a paper on "The Aschheim-Zondek Test in Cutaneous and Mammary Malignant Growths." Discussed by Drs. Milton H. Cohen, York, Pa., and Albert Strickler, Philadelphia.

Dr. Lonie H. Winer, Minneapolis, read a paper on "Pseudo-Epitheliomatous Hyperplasia." Discussed by Drs. Hamilton Montgomery, Rochester, Minn.; Fred D. Weidman, Philadelphia; J. Frank Fraser, New York, and Lonie H. Winer, Minneapolis.

FRIDAY, JUNE 14—MORNING

The chairman appointed the following Committee on Contact Dermatoses: Dr. Earl D. Osborne, Buffalo; Dr. Louis A. Brumsting, Rochester, Minn., and Dr. Edward A. Oliver, Chicago.

The following officers were elected: chairman, Dr. Joseph Gardner Hopkins, New York; vice chairman, Dr. Edward A. Oliver, Chicago; secretary, Dr. C. F. Lehmann, San Antonio, Texas; representative to the Scientific Exhibit, Hamilton Montgomery, Rochester, Minn.; delegate, Dr. Clyde L. Cumner, Cleveland; alternate, Dr. Harold N. Cole, Cleveland; representative to fill the vacancy on the American Board of Dermatology, Dr. C. Guy Lane, Boston.

Dr. Harold N. Cole, Cleveland, stated that the Committee on Scientific Exhibit was to be congratulated on the work it has done, as there have been two honorable mentions and two certificates of merit in this section.

Dr. Herbert L. Traenkle, Buffalo, read a paper on "The Relationship Between Epithelioma Adenoides Cysticum, Trichopilioma and Basal Cell Cancer as Illustrated by Histologic Studies of Multiple Benign Cystic Epithelioma."

Dr. Hyman J. Goldman, St. Louis, read a paper on "Multiple Benign Cystic Epithelioma: Report of Ten Cases in One Family."

These two papers were discussed by Drs. Fred D. Weidman, Philadelphia; Hamilton Montgomery, Rochester, Minn.; Herman Goodman, New York; David Bloom, New York; Richard L. Sutton Jr., Kansas City, Mo.; Herbert L. Traenkle, Buffalo, and Hyman J. Goldman, St. Louis.

Drs. C. W. Enmons, Washington, D. C., and W. Howard Hailey and Hugh Hailey, Atlanta, Ga., presented a paper on "Chromoblastomycosis: Report of the Sixth Case from Continental United States." Discussed by Drs. Joseph Gardner Hopkins, New York; W. M. Sams, Miami, Fla.; Fred D. Weidman, Philadelphia; Morris Moore, St. Louis (by motion extending the privilege of the floor to Dr. Moore), and Hugh Hailey, Atlanta, Ga.

Dr. Leslie M. Smith, El Paso, Texas, read a paper on "Blastomycosis and the Blastomycosis-like Infections." Discussed by Drs. George M. Lewis, New York, and Leslie M. Smith, El Paso, Texas.

Dr. Frederic T. Becker, Duluth, Minn., read a paper on "Milkers' Nodules." Discussed by Drs. M. E. Obermayer, Chicago; C. Guy Lane, Boston, and Frederic T. Becker, Duluth, Minn.

Dr. E. E. Barksdale, Danville, Va., read a paper on "Cutaneous Manifestations from Tobacco with Special Reference to Arsenical Exfoliative Dermatitis." Discussed by Drs. Dudley C. Smith, Charlottesville, Va.; Harry M. Robinson, Baltimore; Marion B. Sulzberger, New York; Herman Sharlit, New York, and E. E. Barksdale, Danville, Va.

Drs. Charles P. Bondurant, Oklahoma City, read a paper on "Adrenal Cortex Extract in the Treatment of Bromide Eruption and Bromide Intoxication." Discussed by Drs. Eugene F. Traub, New York; E. W. Abramowitz, New York; Richard L. Sutton Jr., Kansas City, Mo., and Charles P. Bondurant, Oklahoma City.

The retiring chairman introduced the incoming chairman, Dr. Joseph Gardner Hopkins, New York.

Dr. C. Guy Lane, Boston, moved a vote of thanks to the New York committee and all who were engaged in making this meeting a very successful one, for the entertainment, excellent quarters and luncheon on Thursday. The motion was seconded by Dr. Paul A. O'Leary, Rochester, Minn., and carried.

SECTION ON PREVENTIVE AND INDUSTRIAL MEDICINE AND PUBLIC HEALTH

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the vice chairman, Dr. Clarence D. Selby, Detroit.

Dr. Edgar Mayer, New York, read a paper on "The Clinical Evaluation of Disability in Industrial Pulmonary Diseases." Discussed by Drs. J. Burns Amberson Jr., New York, and Edgar Mayer, New York.

Drs. Robert G. Bloch, William B. Tucker and J. Edmond Bryant, Chicago, presented a paper on "Roentgenologic Group Examinations for Pulmonary Tuberculosis in Negroes in Chicago: A Preliminary Report." Discussed by Drs. Max Pinner, New York; H. R. Edwards, New York; Arthur B. Robins, New York; Haven Emerson, New York, and Robert B. Bloch, Chicago.

Drs. Leonard Greenburg and Adelaide R. Smith, New York, and William T. Siegal, Albany, N. Y., presented a paper on "Medical Aspects of Four Years of Compensation for Silicosis in New York State."

Drs. Arthur M. Master and Simon Dack, New York, presented a paper on "Rehabilitation Following Coronary Occlusion." Discussed by Drs. Harry E. Ungerleider, New York; Cary Eggleston, New York, and Clifford Kuhl, New Haven, Conn.

Dr. H. M. F. Behneman, San Francisco, read a paper on "Should Coronary Disease and Hypertension Be a Cause for Rejection in Industry?" Discussed by Drs. Nelson D. Morris, Toledo, Ohio; Robert T. Legge, Berkeley, Calif.; C. W. Roberts, Atlanta, Ga.; E. J. Stieglitz, Washington, D. C.; Arthur M. Master, New York, and H. M. F. Behneman, San Francisco.

THURSDAY, JUNE 13—AFTERNOON

Dr. Harold S. Diehl, Minneapolis, read the chairman's address, entitled "Medical Careers in Public Health."

Homer N. Calver, New York, read a paper on "Health Information Please." Discussed by Drs. Harrison S. Martland, Newark, N. J.; Millard Knowlton, Hartford, Conn., and Homer N. Calver, New York.

Dr. Charles-Francis Long, Philadelphia, read a paper on "A Program for Industrial Health in State and County Medical Societies." Discussed by Drs. Albert S. Gra, Hartford, Conn., and Charles-Francis Long, Philadelphia.

Dr. Thomas L. Shipman, Lynn, Mass., read a paper on "Opportunities for Physicians in Industry." Discussed by Dr. M. N. Newquist, New York.

Dr. A. Grant Fleming, Montreal, Canada, read a paper on "Preventive Medicine in General Practice." Discussed by Drs. Reginald Fitz, Boston; Haven Emerson, New York; Clifford Kuhl, New Haven, Conn., and A. Grant Fleming, Montreal, Canada.

Dr. M. E. Barnes, Iowa City, read a paper on "Applied Epidemiology in the General Hospital." Discussed by Drs. W. G. Smillie, New York, and Leopold Brahdly, New York.

FRIDAY, JUNE 14—AFTERNOON

Drs. John R. Paul and James D. Trask, New Haven, Conn. presented a paper on "Poliomylitis Virus in Human Stools and in Sewage."

Drs. Howard A. Howe and David Bodian, Baltimore, presented a paper on "The Portal of Entry in Poliomylitis."

Dr. W. Lloyd Aycock, Boston, read a paper on "The Frequency of Poliomylitis in Pregnancy."

These three papers were discussed by Drs. James P. Leake, Washington, D. C.; T. M. Rivers, New York; Harold L. Amoss, Greenwich, Conn.; James D. Trask, New Haven, Conn., and Howard A. Howe, Baltimore.

The following officers were elected: chairman, Dr. Clarence D. Selby, Detroit; vice chairman, Dr. Huntington Williams, Baltimore; secretary, Dr. W. A. Sawyer, Rochester, N. Y.; executive committee: Dr. I. C. Riffin, Richmond, Va.; Dr. Harold S. Diehl, Minneapolis, and Dr. Clarence D. Selby, Detroit; chairman, Committee on Section Exhibit, Dr. P. A. Davis, Akron, Ohio.

Dr. Lowell S. Selling, Detroit, read a paper on "The Mental Hygiene Aspect of the Traffic Accident." Discussed by Dr. Daniel Blain, New York.

Drs. Murray B. Ferderber and F. C. Houghten, Pittsburgh, presented a paper on "Effective Temperature Scale: A Measure of Human Comfort in Environmental Temperature." Discussed by Dr. W. J. McConnell, New York.

SECTION ON UROLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2:05 by the chairman, Dr. Frederic E. B. Foley, St. Paul.

Drs. William F. Braasch, Waltman Walters and Howard J. Hammer, Rochester, Minn., presented a paper on "Hypertension and the Surgical Kidney."

Drs. E. Granville Crabtree and Nathan Chaset, Boston, presented a paper on "A Combined Clinical and Clinicopathologic Study of 150 Nephrectomized Patients in Respect to Vascular Nephritis and Hypertension."

These two papers were discussed by Drs. Stanford W. Mulholland, Philadelphia; Roy J. Holmes, Miami, Fla.; Earl E. Ewert, Boston; James F. McCahey, Philadelphia; George W. Fish, New York; William F. Braasch, Rochester, Minn., and Nathan Chaset, Boston.

Drs. Budd C. Corbus and Budd C. Corbus Jr., Chicago, presented a paper on "The Cutaneous Diagnosis of Gonococcal Infections Illustrated with Kodachrome Transparencies: A Further Report." Discussed by Drs. Michael Wishengrad, New York; John H. Morrissey, New York, and Budd C. Corbus, Chicago.

Dr. Russell D. Herrold, Chicago, read a paper on "Chemotherapy in the Treatment of Gonorrhea."

Drs. Edwin P. Alyea, Durham, N. C., read a paper on "The Present Status of Chemotherapy in Nonspecific Infections of the Urinary Tract."

Drs. Grayson L. Carroll, Louis C. Kappel and Bransford Lewis, St. Louis, presented a paper on "Therapy with the Thiazole Compounds of Sulfanilamide."

These three papers were discussed by Drs. Charles A. W. Uhle, Philadelphia; V. Rogers Deakin, St. Louis; P. S. Pelouze, Philadelphia; W. Ray Jones, Seattle; Reed M. Nesbit, Ann Arbor, Mich., and Russell D. Herrold, Chicago.

THURSDAY, JUNE 13—AFTERNOON

Dr. Frederic E. B. Foley, St. Paul, read the chairman's address, entitled "Surgical Correction of Horseshoe Kidney."

Dr. Hugh H. Young, Baltimore, read a paper on "Pathology and Surgical Treatment of Vesical Neck Obstruction in Women." Discussed by Drs. Henry Dawson Furniss, New York; Alf H. Gundersen, La Crosse, Wis.; Edward N. Cook, Rochester, Minn.; T. Leon Howard, Denver, and Hugh H. Young, Baltimore.

Drs. H. M. Stang and A. J. Hertzog, Eau Claire, Wis., presented a paper on "Primary Carcinoma of the Ureter: A Report of Four Cases."

Drs. Edward N. Cook and Virgil S. Counseller, Rochester, Minn., presented a paper on "Primary Epithelioma of the Ureter."

These two papers were discussed by Drs. Paul A. Ferrier, Pasadena, Calif.; Monroe E. Greenberger, New York; Hugh H. Young, Baltimore; T. Leon Howard, Denver, and Virgil S. Counseller, Rochester, Minn.

Dr. James C. Sargent, Milwaukee, read a paper on "Injury of the Kidneys with Special Reference to Early and Accurate Diagnosis Through Pyelography." Discussed by Drs. Roy B. Henline, New York; George F. Cahill, New York; William Calhoun Stirling, Washington, D. C.; Vincent J. O'Connor, Chicago, and James C. Sargent, Milwaukee.

Dr. Edwin Davis, Omaha, read a paper on "Technic and Results in Perineal Prostatectomy" and showed a motion picture of the operation. Discussed by Drs. Oswald Swinney Lowsley, New York; Hugh H. Young, Baltimore, and Edwin Davis, Omaha.

The chairman announced that in the elections for the coming year three urologists had been elected to offices in the American

Medical Association: Dr. Herman L. Kretschmer, Chicago, treasurer; Dr. William F. Braasch, Rochester, Minn., to the Board of Trustees, and Dr. Parke G. Smith, Cincinnati, vice president.

FRIDAY, JUNE 14—AFTERNOON

The following officers were elected: chairman, Dr. Meredith F. Campbell, New York; vice chairman, Dr. L. F. Huffman, Cleveland; secretary, Dr. Vincent J. O'Connor, Chicago; delegate, Dr. Hermon C. Bumpus Jr., Pasadena, Calif., and alternate, Dr. George C. Prather, Boston.

The chairman read the following recommendation from the executive committee: In the past there has been no recorded stipulation or approved precedent covering the nominations of our representatives for election by the American Board of Urology, Inc., to its membership. The nomination of none of our present representatives on the board has had approval by vote of the section.

Your executive committee recommends that in the future its nominations for election of representatives by the American Board of Urology, Inc., to its membership be submitted to the members of the section for approval by vote.

On motion by Dr. Grayson L. Carroll, St. Louis, seconded by Dr. T. Leon Howard, Denver, the recommendation was adopted.

The chairman asked the secretary to present nominations of the executive committee for membership on the Board of Urology, stating that there were two places to be filled.

The secretary stated that he would like to acquaint the section with the present status of the American Board of Urology, Inc., constitution, which had been changed during the past year as regards election of members of the board, and further stated: I have been confronted as secretary with a situation where there has been considerable confusion as to what constituted a legal and acceptable nomination of this section to the board. After an extensive research, I found no recorded procedure either in the previous minutes of the section or definite data from the American board itself. For this reason the executive committee felt that, in order to make the selection of our men to the American board without question as far as the executive committee is concerned, the recommendation which the chairman just read should be made. The executive committee feels that the selection of these men should be a part of the regular procedure of this section and that every one should have a voice in the matter, and in that way every one will feel that he is having a part in selecting representative men to represent this section on the board.

Prior to this year the executive committee has selected one man, whose name has been sent to the American board. During the past year the American board has changed its method of selecting from this section and others.

The secretary then read from correspondence from the American Board of Urology, Inc., regarding the method of selecting members, as follows:

Each nominating society may submit to the board of trustees the names of not less than three of their eligible member physicians as its nominees in the alternative, for each successor membership to which a nominee of such nominating society shall be eligible for election, but if any such nominating society shall fail so to submit the names of three or more such nominees not later than ten days prior to the meeting of the members, annual or special, at which the election of such successor member is scheduled to take place, or if no such nominee shall receive sufficient votes to elect him to membership, then, and in either such event, the board of trustees, by a majority vote, may designate any eligible member of such nominating society as the nominee of such nominating society for election to such successor membership of this corporation.

The section then voted to recommend the following nominations for the American Board of Urology, Inc.:

For a four year term: Dr. Clarence G. Bandler, New York; Dr. Frank Hinman, San Francisco; Dr. Miley B. Wesson, San Francisco.

For a five year term: Dr. Alfred I. Folsom, Dallas, Texas; Dr. Albert E. Goldstein, Baltimore; Dr. Thomas D. Moore, Memphis, Tenn.

Dr. Henry A. R. Kreutzmann, San Francisco, read a paper on "Sterility in the Male: Diagnosis and Treatment."

Drs. Samuel R. Meaker and Samuel N. Vose, Boston, presented a paper on "The Nature of Human Infertility."

Dr. Charles W. Charny, Philadelphia, read a paper on "Testicular Biopsy: Its Value in Male Sterility."

Dr. Francis R. Hagner, Washington, D. C., read a paper on "The Operative Treatment of Sterility in the Male: Further Report, with Table of Results in Eighty-Five Cases."

These four papers were discussed by Drs. Robert S. Hotchkiss, New York; Max Huhner, New York; Henry Sangree, Philadelphia; W. W. Williams, Springfield, Mass.; Henry A. R. Kreutzmann, San Francisco; Charles W. Charny, Philadelphia, and Francis R. Hagner, Washington, D. C.

Drs. Bernard Strauss and Gerson R. Biskind, San Francisco, presented a paper on "The Implantation of Pellets of Methyl Testosterone in the Treatment of Eunuchoidism."

Dr. Walter M. Kearns, Milwaukee, read a paper on "The Oral Administration of Methyl Testosterone in Testicular Deficiency."

These two papers were discussed by Drs. Norris J. Heckel, Chicago; Samuel A. Vest Jr., Charlottesville, Va.; William P. Herbst Jr., Washington, D. C.; Charles W. Dunn, Philadelphia; Bernard Strauss, San Francisco, and Walter M. Kearns, Milwaukee.

The secretary expressed the thanks and appreciation of the section to the New York committee, Dr. Clarence G. Bandler, Dr. Roy B. Henline, Dr. Francis N. Kimball and Dr. Meredith F. Campbell, for their splendid cooperation in making the meeting a success.

SECTION ON ORTHOPEDIC SURGERY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Robert V. Funsten, Charlottesville, Va.

Drs. William B. Carrell Jr. and Brandon Carrell, Dallas, Texas, presented a paper on "Fractures of the Neck of the Femur in Children." Discussed by Drs. Mark H. Rogers, Boston; James A. Dickson, Cleveland; Francis M. McKeever, Los Angeles, and William B. Carrell Jr., Dallas, Texas.

Dr. James E. M. Thomson, Lincoln, Neb., read a paper on "A Program for the Treatment of Compound Fractures." Discussed by Drs. Robert W. Johnson Jr., Baltimore; Donald E. McKenna, Brooklyn; Myron O. Henry, Minneapolis; Harold R. Bohlman, Baltimore, and James E. M. Thomson, Lincoln, Neb.

Drs. G. Mosser Taylor and Alonzo J. Neufeld, Los Angeles, presented a paper on "External or Internal Fixation for Inter-trochanteric Fractures." Discussed by Drs. Frank M. Hand, Washington, D. C.; Armitage Whitman, New York; Abraham M. Rechtman, Philadelphia, and G. Mosser Taylor, Los Angeles.

A nominating committee was appointed, consisting of Drs. James E. M. Thomson, Lincoln, Neb., chairman; Ralph Ghormley, Rochester, Minn.; W. Barnett Owen, Louisville, Ky., and Philip Lewin, Chicago.

Dr. Jesse T. Nicholson, Philadelphia, read a paper on "Spontaneous Reduction of Cervical Spine Dislocation in Children." Discussed by Drs. William H. Von Lackum, New York; Barbara B. Stimson, New York, and Jesse T. Nicholson, Philadelphia.

Dr. Charles R. Rountree, Oklahoma City, read a paper on "Diaphysectomy for Chronic Osteomyelitis of the Fibula." Discussed by Drs. John R. Cobb, New York, and Charles R. Rountree, Oklahoma City.

Dr. Howard A. Swart, Charleston, W. Va., read a paper on "The Use of Double Wire Traction in the Treatment of Fractures of the Shaft of the Femur." Discussed by Drs. George W. Van Gorder, Boston; Clay Ray Murray, New York; John P. Stump, New York, and Howard A. Swart, Charleston, W. Va.

THURSDAY, JUNE 13—AFTERNOON

Dr. Hira E. Branch, Detroit, read a paper on "Progressive Pseudohypertrophic Muscular Dystrophy: A New Regimen of Treatment." Discussed by Drs. Joseph B. L'Episcopo, Brooklyn; Joseph A. Freiberg, Cincinnati; Ralph K. Ghormley, Rochester, Minn., and Hira E. Branch, Detroit.

The following officers were elected: chairman, J. Albert Key, St. Louis; vice chairman, James A. Dickson, Cleveland; secre-

tary, Guy A. Caldwell, New Orleans; executive committee Oscar L. Miller, Charlotte, N. C.; Robert V. Funsten, Charlottesville, Va., and J. Albert Key, St. Louis; delegate, Jan Archer O'Reilly, St. Louis; alternate, William B. Carrell, Dallas, Texas; nominees to the American Board of Orthopedic Surgery, James S. Speed, Memphis, Tenn., and Frank R. O'Brien, Boston.

Dr. Gilbert E. Haggart, Boston, read a paper on "Ear Operation (Spine Fusion) in Unstable Lumbosacral Joints Discussed by Drs. Allen F. Voshell, Baltimore; Frederick J. Jostes, St. Louis, and Gilbert E. Haggart, Boston.

Dr. Robert V. Funsten, Charlottesville, Va., read the chairman's address, entitled "Problems in Fractures of the Lower Third of the Femur."

Dr. Frank G. Murphy, Chicago, read a paper on "Surgical Closure of Osseous Tuberculous Abscesses." Discussed by Dr. Robert J. Cook, New Haven, Conn.; John R. Cobb, New York, and Frank G. Murphy, Chicago.

Dr. Harold R. Bohlman, Baltimore, read a paper on "An Improved Technic for Removal of the Semilunar Cartilage and the Postoperative Treatment." Discussed by Drs. Al DeForest Smith, New York; Philip Lewin, Chicago, and Harold R. Bohlman, Baltimore.

Dr. James Archer O'Reilly, St. Louis, delegates to the House made a report on the session of the House of Delegates, which was accepted.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Surgery General and Abdominal. The proceedings are reported in the minutes of that section.

SECTION ON GASTRO-ENTEROLOGY AND PROCTOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman Dr. A. H. Aaron, Buffalo.

Drs. Abraham J. Gitlitz, Englewood, N. J., and Henry H. Lerner, Boston, presented a paper on "Interpretation of Gastroscopic Observations in Terms of Mucosal Changes: Histologic Study."

Dr. Chester M. Jones, Boston, read a paper on "Clinical and Therapeutic Implications of Gastritis."

These two papers were discussed by Drs. Burrill B. Crohn, New York; Herman J. Moersch, Rochester, Minn.; Alfred S. White, San Francisco; Allan L. Cohn, San Francisco; Julian M. Ruffin, Durham, N. C.; William A. Swalm, Philadelphia; Lester M. Morrison, Philadelphia; Abraham J. Gitlitz, Englewood, N. J., and Chester M. Jones, Boston.

Dr. Frank C. Val Dez, Chicago, read a paper on "The Night Secretion of Hydrochloric Acid in the Stomach."

Drs. Herbert C. Breuhaus and James B. Eyerly, Chicago, presented a paper on "Antacids: Their Reaction by Titration and Within the Human Stomach."

These two papers were discussed by Drs. Moses Einhorn, New York; Harry Gauss, Denver; David J. Sandweiss, Detroit; Asher Winkelstein, New York; V. C. Rowland, Cleveland; Isidor Greenwald, New York; Leo L. Hardt, Chicago; John M. Blackford, Seattle; Walter L. Palmer, Chicago; Herbert C. Breuhaus, Chicago, and Frank C. Val Dez, Chicago.

Drs. Russell S. Boles, Helena E. Riggs, and John O. Griffith, Philadelphia, presented a paper on "Neurogenic Factors in Production of Peptic Ulcer."

Drs. Leon Schiff, Richard J. Stevens and Harold K. Moss, Cincinnati, presented a paper on "The Prognostic Significance of the Blood Urea Nitrogen Following Hematemesis or Melena."

Drs. Clarence E. Bird, Providence, R. I., Margaret A. Limper, Louisville, Ky., and Jacob M. Mayer, Mayfield, Ky., presented a paper on "Surgery in Peptic Ulcer of Infants and Children."

Dr. John M. Blackford, Seattle, read a paper on "Fatal Hemorrhage from Peptic Ulcer."

These four papers were discussed by Drs. Walter L. Palmer, Chicago; Sidney Leibowitz, New York; Julius Chasnoff, New York; Irving Gray, Brooklyn; Burrill B. Crohn, New York; Arthur W. Allen, Boston; Andrew B. Rivers, Rochester, Minn.; Hyman I. Goldstein, Camden, N. J.; Anthony Bassler, New

York; Henry N. Harkins, Detroit; Horace W. Soper, St. Louis; Leon Bloch, Chicago; Harry L. Segal, Rochester, N. Y.; I. R. Jankelson, Boston; Frederick W. Mulow, Cedar Rapids, Iowa; Russell S. Boles, Philadelphia; Helena E. Riggs, Philadelphia; Leon Schiff, Cincinnati; Clarence E. Bird, Providence, R. I., and John M. Blackford, Seattle.

THURSDAY, JUNE 13—MORNING

Drs. Donovan C. Browne and George Gordon McHardy, New Orleans, presented a paper on "Primary Jejunal Pathology." Discussed by Drs. David Adlersberg, New York; Maurice Feldman, Baltimore, and Donovan C. Browne, New Orleans.

Drs. E. G. Wakefield and N. T. Friedell, Rochester, Minn., presented a paper on "The Structural Significance of the Ileocecal Valve." Discussed by Drs. Ernest H. Gaither, Baltimore; Jacob M. Ravid, New York, and E. G. Wakefield, Rochester, Minn.

Drs. Maurice M. Rothman and Harry J. Epstein, Philadelphia, presented a paper on "A Clinical Entity Associated with the So-Called Nonpathogenic Ameba." Discussed by Drs. Asher Winkelstein, New York; Horace W. Soper, St. Louis; Palmer Dysart, Phoenix, Ariz.; Moses Paulson, Baltimore; Anthony Bassler, New York, and Maurice M. Rothman, Philadelphia.

Drs. Jacob Gershon-Cohen and Harry Shay, Philadelphia, presented a paper on "Carcinoma of the Colon: Early Diagnosis with Double Contrast Enema." Discussed by Drs. E. C. Koenig, Buffalo; Louis J. Hirschman, Detroit; B. R. Kirklin, Rochester, Minn., and Jacob Gershon-Cohen, Philadelphia.

Drs. Leo L. Hardt and Seymour J. Cohen, Chicago, presented a paper on "Gastrointestinal Complications in Pulmonary Tuberculosis." Discussed by Drs. Joseph Felsen, New York; Julius Friedenwald, Baltimore; Russell S. Boles, Philadelphia; Emil Granet, New York; Clement L. Martin, Chicago; Henry L. Bockus, Philadelphia, and Leo L. Hardt, Chicago.

Dr. Sara M. Jordan, Boston, read a paper on "End Results in Radical Gastrointestinal Surgery as Seen by the Gastro-Enterologist." Discussed by Drs. John G. Mateer, Detroit; Henry L. Bockus, Philadelphia; A. H. Aaron, Buffalo, and Sara M. Jordan, Boston.

Dr. Harry E. Bacon, Philadelphia, read a paper on "Anorectal Operative Procedures with Special Reference to the Avoidance of Pain, Based on a Series of 1,000 Cases." Discussed by Drs. Emil Granet, New York; Henry Raile, Salt Lake City; Malcolm R. Hill, Los Angeles; Louis J. Hirschman, Detroit; Arthur S. Calman, New York, and Harry E. Bacon, Philadelphia.

Dr. Horace W. Soper, St. Louis, read a paper on "Megacolon." Discussed by Drs. Sara M. Jordan, Boston; J. Arnold Bargen, Rochester, Minn., and Horace W. Soper, St. Louis.

FRIDAY, JUNE 14—MORNING

The following officers were elected: chairman, Dr. Frank C. Yeomans, New York; vice chairman, Dr. Walter L. Palmer, Chicago; secretary, Dr. J. Arnold Bargen, Rochester, Minn.; executive committee, Dr. Descum C. McKenney, Buffalo; Dr. A. H. Aaron, Buffalo, and Dr. Frank C. Yeomans, New York; delegate, Dr. Louis A. Buie, Rochester, Minn.; alternate, Dr. Emmett H. Terrell, Richmond, Va.; chairman of Committee on Section Exhibit, Dr. Sara M. Jordan, Boston.

Drs. William Bennett Bean and Tom Douglas Spies, Cincinnati, presented a paper on "Vitamin Deficiencies in Diarrheal States."

Dr. Garnett Cheney, San Francisco, read a paper on "The Clinical Value of Vitamin K."

These two papers were discussed by Drs. Thomas T. Mackie, New York; Donald T. Chamberlin, Boston; Mandred W. Comfort, Rochester, Minn.; John L. Kantor, New York; William Bennett Bean, Cincinnati, and Garnett Cheney, San Francisco.

Dr. Mandred W. Comfort, Rochester, Minn., read a paper on "The Use and Significance of Tests of Pancreatic Function."

Dr. Jacob Meyer, Chicago, read a paper on "The Clinical Significance of Salivary, Gastric and Pancreatic Secretion in Old Age."

These two papers were discussed by Drs. Joseph S. Diamond, New York; A. C. Ivy, Chicago; Edward S. Emery Jr., Boston;

John L. Kantor, New York; Heinrich Necheles, Chicago; A. H. Aaron, Buffalo; Mandred W. Comfort, Rochester, Minn., and Jacob Meyer, Chicago.

Drs. Maurice Feldman and Samuel Morrison, Baltimore, presented a paper on "The Management of Gallbladder Based on a Cholecystographic Classification."

Dr. Moses Behrend, Philadelphia, read a paper on "Diseases of the Common Bile Duct and Its Relation to the Gastro-intestinal Tract."

Dr. Emmanuel Deutsch, Boston, read a paper on "A Fractional Bromsulphalein Test Compared to Other Liver Function Tests for Residual Liver Damage."

These three papers were discussed by Drs. Max Thorek, Chicago; Moses Paulson, Baltimore; J. Russell Twiss, New York; Julius Friedenwald, Baltimore; S. Allen Wilkinson Jr., Boston; Mandred W. Comfort, Rochester, Minn.; A. J. Atkinson, Chicago; Henry A. Rafsky, New York; A. F. R. Andresen, Brooklyn; Maurice Feldman, Baltimore; Moses Behrend, Philadelphia, and Emmanuel Deutsch, Boston.

SECTION ON RADIOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman, Dr. Merrill C. Sosman, Boston.

Dr. Lyndon E. Lee Jr., Wrentham, Mass., read a paper on "Medication in the Control of Pain in Terminal Cancer with Reference to the Study of Newer Synthetic Analgesics." Discussed by Drs. David I. Macht, Baltimore, and Lyndon E. Lee Jr., Wrentham, Mass.

Dr. Francis C. Grant, Philadelphia, read a paper on "Surgical Methods for the Relief of Pain." Discussed by Drs. Byron Stookey, New York, and Francis C. Grant, Philadelphia.

Drs. Eugene T. Leddy and Herman J. Moersch, Rochester, Minn., presented a paper on "Roentgen Therapy for Bronchiogenic Carcinoma." Discussed by Dr. Maurice Lenz, New York.

Dr. William Stuart Wallace, Durham, N. C., read a paper on "Studies in Radiation Sickness: Variations in the Intestinal Pattern in Sickness Accompanying Protracted Irradiation of Deep-Seated Tumors." Discussed by Drs. Ross Golden, New York; Virgil H. Moon, Philadelphia; Morton L. Levin, Albany, N. Y., and William Stuart Wallace, Durham, N. C.

Drs. Virgil H. Moon, Karl Kornblum and David R. Morgan, Philadelphia, presented a paper on "The Nature and Pathology of Radiation Sickness." Discussed by Drs. Charles L. Martin, Dallas, Texas; David I. Macht, Baltimore; Ross Golden, New York; Moses F. Lubell, Waterville, Maine; Robert P. Noble, Raleigh, N. C., and Virgil H. Moon, Philadelphia.

Dr. William E. Costolow, Los Angeles, read a paper on "Treatment of Uterine Fibromyomas." Discussed by Drs. William P. Healey, New York; Channing W. Barrett, Chicago; Arthur H. Curtis, Chicago, and William E. Costolow, Los Angeles.

THURSDAY, JUNE 13—MORNING

The following officers were elected: chairman, Dr. Raymond C. Beeler, Indianapolis; vice chairman, Dr. Ralph S. Bromer, Bryn Mawr, Pa.; secretary, Dr. John T. Murphy, Toledo, Ohio; delegate, Dr. Edward H. Skinner, Kansas City, Mo.; alternate, Dr. Eugene P. Pendergrass, Philadelphia; representative to the Board of Radiology, Dr. George W. Holmes, Boston.

Dr. Merrill C. Sosman, Boston, read the chairman's address, entitled "Subclinical Mitral Disease."

Dr. Robert E. Gross, Boston, read a paper on "Experiences with Surgical Treatment of the Patent Ductus Arteriosus: A Summary of Nine Cases." Discussed by Dr. Claude S. Beck, Cleveland.

Drs. Eugene C. Eppinger and C. Sidney Burwell, Boston, presented a paper on "The Mechanical Effects of Patent Ductus Arteriosus on the Heart and Their Relation to X-Ray Signs." Discussed by Drs. William D. Stroud, Philadelphia; Harry Vesell, New York; Maude E. S. Abbott, Montreal; M. J. Shapiro, Minneapolis; Harold E. B. Pardee, New York; William J. Kerr, San Francisco; Arthur E. Strauss, St. Louis; Robert E. Gross, Boston, and C. Sidney Burwell, Boston.

Dr. Marshall N. Fulton, Boston, read a paper on "Aneurysm of the Ventricle of the Heart." Discussed by Drs. William J. Kerr, San Francisco; Emanuel Libman, New York; Simon Dack, New York, and Marshall N. Fulton, Boston.

Dr. Soma Weiss, Boston, read a paper on "The Heart in Nutritional Deficiencies." Discussed by Drs. Tom Douglas Spies, Cincinnati, and Norman H. Jolliffe, New York.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Laryngology, Otolaryngology.

Dr. Harris P. Mosher, Boston, read a paper on "Fulminating Osteomyelitis of the Frontal Bone as a Complication of Infection of the Frontal Sinus."

Dr. A. S. MacMillan, Boston, read a paper on "Radiologic Aspects of Osteomyelitis of the Frontal Bone."

These two papers were discussed by Drs. Arthur C. Jones, Boise, Idaho; Joseph E. J. King, New York; Samuel R. Skillern Jr., Philadelphia; Cornelius G. Dyke, New York; Harris P. Mosher, Boston, and A. S. MacMillan, Boston.

Dr. Gordon F. Harkness, Davenport, Iowa, read a paper on "The Complications of Acute Mastoid Surgery."

Dr. Vincent C. Johnson, Ann Arbor, Mich., read a paper on "Roentgen Signs of Mastoiditis and Its Complications."

These two papers were discussed by Drs. Isidore Friesner, New York; Frederick M. Law, New York; Gordon F. Harkness, Davenport, Iowa, and Vincent C. Johnson, Ann Arbor, Mich.

Dr. Charles L. Martin, Dallas, Texas, read a paper on "Radiologic Treatment of Metastatic Cervical Lymph Nodes." Discussed by Drs. James J. Duffy, New York; Douglas Quick, New York; C. A. Whitcomb, Philadelphia, and Charles L. Martin, Dallas, Texas.

SECTION ON MISCELLANEOUS TOPICS

Session on Anesthesia

THURSDAY, JUNE 13—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Paul M. Wood, New York.

Dr. Paul M. Wood, New York, read the chairman's address.

Drs. Stuart C. Cullen, S. E. Ziffren, R. B. Gibson and H. P. Smith, Iowa City, presented a paper on "Anesthesia and Laceration Injury with Special Reference to Plasma Prothrombin Levels." Discussed by Drs. Huberta M. Livingstone, Chicago; Milton C. Peterson, New York; Max H. Weinberg, Pittsburgh, and Stuart C. Cullen, Iowa City.

Drs. E. A. Rovenstine and John Adriani, New York, presented a paper on "Studies on the Absorption of Carbon Dioxide from Anesthetic Mixtures." Discussed by Drs. Ralph J. Waters, Madison, Wis., and John Adriani, New York.

Drs. Ralph M. Tovell and Charles B. Hinds Jr., Hartford, Conn., presented a paper on "Abdominal Blocks in Conjunction with General Anesthesia for Upper Abdominal Surgery." Discussed by Drs. John S. Lundy, Rochester, Minn.; Robert Patterson, Pittsburgh, and Ralph M. Tovell, Hartford, Conn.

Dr. Lloyd H. Mousel, Rochester, Minn., read a paper on "The Anesthetist's Part and Opportunity in the Diagnosis and Treatment of Postoperative Atelectasis." Discussed by Drs. U. Eversole, Boston; Herman J. Moersel, Rochester, Minn.; F. Elmore Hubbard, Montclair, N. J., and Lloyd H. Mousel, Rochester, Minn.

Dr. Meyer Saklad, Providence, R. I., read a paper on "Criteria in the Choice of Anesthesia." Discussed by Drs. A. H. Mill, Providence, R. I.; Charles F. McCuskey, Glendale, Calif.; and Meyer Saklad, Providence, R. I.

WOMAN'S AUXILIARY

Louisiana

The auxiliary to the Orleans Parish Medical Society elected Mrs. A. F. Herbert president for 1940. During the past year the auxiliary was hostess to the doctors' wives who attended the meeting of the American College of Physicians and the meeting of the New Orleans Graduate Assembly. The auxiliary also assisted in entertaining visitors to the Southern Sectional Meeting of the American College of Surgeons in New Orleans January 17-19. The auxiliary has collected funds to help a physician's widow who was in need.

New Hampshire

The woman's auxiliary to the New Hampshire Medical Society held its fifteenth annual meeting in Manchester, May 14-15; among the speakers were Dr. Nathan B. Van Etten, President-Elect of the American Medical Association; Dr. George C. Wilkins, president, New Hampshire State Board of Health, Manchester, who discussed the "Benevolence Fund of the New Hampshire Medical Society," and Kenneth N. Atkins, M.A., professor of bacteriology at Dartmouth Medical School, Hanover, N. H.

Ohio

An auxiliary to the Ohio State Medical Association was organized in Cincinnati, May 15. Mrs. David W. Thomas, Lock Haven, Pa., first vice president and chairman, organization committee, Woman's Auxiliary to the American Medical Association, addressed more than 100 women at the organization meeting. The officers elected for the new organization were: Mrs. J. E. Purdy, Canton, president; Mrs. Horace Tangeman, Cincinnati, first vice president; Mrs. J. L. Stevens, Mansfield, secretary-treasurer.

Pennsylvania

At a meeting of the auxiliary to the Chester County Medical Society in West Chester, January 16, Mrs. Joseph Scattergood Sr. reviewed "The Tree of Life," by Elizabeth Page.

Major Edward A. Davies, 315th Infantry Reserve, gave an address on "The European Kaleidoscope" before a joint meeting of the Delaware County Medical Society and its auxiliary in Chester recently. The auxiliary has donated subscriptions to *Hygeia* to public reading centers in Delaware County.

At a recent meeting of the auxiliary to the Lycoming County Medical Society in Williamsport, Mr. Joseph Schmucker and Mr. Theodore Walters of the Williamsport Police Department spoke on fingerprinting, giving illustrations by means of slides and photographs.

At a recent meeting of the auxiliary to the Philadelphia County Medical Society, Dr. Myer Solis-Cohen spoke on medical benevolence; other recent guest speakers have been Mrs. John H. Doane, president of the auxiliary to the Medical Society of the State of Pennsylvania; Dr. Francis F. Borzell, president-elect of the Medical Society of the State of Pennsylvania, and Miss Besse Howard, director of the Pennsylvania Branch of the League of Nations Association.

The auxiliary to the Dauphin County Medical Society met in Harrisburg February 27. Dr. Eleanor R. Stein discussed the value of regular physical examinations on school children.

Mrs. John H. Doane, president of the auxiliary to the Medical Society of the State of Pennsylvania, spoke on the work of the auxiliary at a joint meeting of the auxiliaries to the Tioga and Bradford County medical societies in Troy.

The woman's auxiliary to the Lehigh County Medical Society recently donated \$100 to the Allentown Community Chest, \$25 to Girl's Haven, a recreational center for underprivileged girls, and \$10 to the Red Cross Relief Fund; the auxiliary also secured 312 subscriptions to *Hygeia* during the recent Hygeia campaign; at a past president's party in April, twenty-one past presidents of the auxiliary were present.

Dr. and Mrs. Augustus S. Kech, Altoona, entertained the Blair County Medical Society and its auxiliary in honor of Mrs. Rollo K. Packard, president of the auxiliary to the American Medical Association, January 17.

West Virginia

Miss Dorothea Campbell, of the West Virginia State Health Department, spoke on state health laws at the January meeting of the auxiliary to the Kanawha County Medical Society in Charleston; thirty-five members attended.

Mrs. Harold H. Golz spoke on the prevalence, symptoms and diagnosis of cancer at a meeting of the auxiliary to the Harrison County Medical Society, Clarksburg, January 4.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Society News.—The Craighead-Poinsett County Medical Society was addressed recently by Drs. Duane M. Carr and Conley H. Sanford, both of Memphis, Tenn., on "Role of Amebiasis in Chronic Digestive Disturbances" and "Injuries to the Chest" respectively.—Dr. Richard E. Ching, Memphis, discussed "Blood Pressure" before the Mississippi County Medical Society, May 7, and Dr. Gilbert J. Levy, Memphis, "Certain Drugs in the Treatment of Meningitis."—The speakers before the Benton County Medical Society in Gentry, May 9, were Drs. Roy E. Myers and A. M. Gregg, both of Joplin, Mo., on hyperinsulinism and hyperthyroidism, respectively.

CALIFORNIA

Sale of Sobisminol Restricted.—Because of the dangers involved in self administration of sobisminol, the California State Board of Health has adopted regulations that prohibit the sale of the drug except on written prescription of a duly licensed physician. Manufacturers of the product are also required to provide full information relative to the use of the drug in their products.

Another Symphony Orchestra.—The *Bulletin* of the San Francisco County Medical Society announces the recent formation of a "Doctors' Symphony Orchestra." Officers are Drs. Joseph L. McCool, president; Leo Eloesser and J. F. Steffan, D.D.S., vice presidents, and Dr. Donald R. Pratt, secretary-treasurer, all of San Francisco. About thirty-five physicians and dentists attended the first rehearsal at the home of the county medical society, May 16.

New State Director of Health.—Dr. Bertram P. Brown, Los Angeles, has been appointed director of the California State Department of Public Health to succeed Dr. Walter M. Dickie, San Francisco. Dr. Brown graduated at University and Bellevue Hospital Medical College, New York, in 1914. He is 48 years of age. Dr. Dickie served as chief of the division of venereal disease control in 1919, but this activity ceased in 1920 on account of lack of funds, according to *California and Western Medicine*. In 1920 he was named secretary and executive officer of the state board of health, holding this title until 1929, when he was appointed director of public health. He held this position until 1931. In 1935 he was again named health director.

DISTRICT OF COLUMBIA

Annual Meeting of Former Interns.—The twenty-first annual session of the Association of Former Interns of Freedmen's Hospital was held at the hospital, Washington, June 4-6. The speakers included:

- Dr. Harry Maceo Williams, Baltimore, The Druid Health Center.
- Dr. Harry M. Robinson, Baltimore, Reactions from the Arsenicals.
- Dr. Joseph E. Moore, Baltimore, Determination of Cure in Syphilis.
- Dr. William Montague Cobb, Erect Posture as a Key to Human Anatomy.
- Dr. Samuel L. Bullock, Cases Illustrating Pitfalls in the Diagnosis of Appendicitis.
- Dr. George M. Leiby, Epidemiology of Syphilis.
- Dr. Perrin H. Long, Baltimore, Clinical Evaluation of the Use of Sulfanilamide, Neoprontosil, Sulfapyridine and Sulfathiazole in the Treatment of Infections.
- Dr. Richard W. TeLinde, Baltimore, Organic Causes of Uterine and Genital Bleeding.
- Dr. Charles R. Drew, Controlled Fluid Therapy.
- Dr. Paul F. Dickens, Diagnosis and Treatment of the Anemias.
- Dr. Edward Gaylord Howell, New Brunswick, N. J., Treatment of Chronic Alcoholism.

FLORIDA

State Medical Election.—Dr. Walter C. Jones Jr., Miami, was chosen president-elect of the Florida Medical Association at its recent annual session and Dr. John S. Turberville, Century, was inducted into the presidency. Vice presidents are Drs. John R. Boling, Tampa; Ferdinand Richards, Jacksonville, and Erasmus B. Hardee, Vero Beach, and Dr. Shaler A. Richardson, Jacksonville, was reelected secretary-treasurer. The 1941 meeting will be in Jacksonville.

Drs. Arce and Campos Honored.—A fishing party and dinner was given in Venice, June 7, by Dr. Fred H. Albee in honor of Dr. José Arce, dean of the faculty of medical science and professor of the surgical clinic, University of Buenos Aires,

Argentina, and Dr. Oswaldo P. Campos, orthopedic surgeon of Rio de Janeiro. Among the guests were Drs. Frank D. Dickson, Kansas City, Mo.; Oscar L. Miller, Charlotte, N. C.; Edward William Alton Ochsner, New Orleans, and Joseph F. McCarthy, New York. Dr. Arce will preside at the next congress of the Pan American Medical Association in Buenos Aires, August 1941, at which time the new medical school of the University of Buenos Aires will be opened.

GEORGIA

Fifty Years of Practice.—Dr. William R. Camp, Fairburn, celebrated his fiftieth year in the practice of medicine recently. —Recently Dr. Robert E. Adair, Cartersville, marked his completion of fifty years in the practice of medicine.

District Meeting.—The Seventh District Medical Society was addressed in Cedartown recently, among others, by Drs. Ben H. Clifton, Atlanta, on "Management and Treatment of Lung Abscesses"; Joseph Yampolsky, Atlanta, "Present Status of Chemotherapy in Pneumococcal Infections with Special Emphasis on the Use of Sulfapyridine and Sulfathiazole," and Robert F. Norton, Rome, "Etiologic Factors of Human Sterility in the Male."

Public Health Meeting.—The Georgia Public Health Association held its annual meeting at the Ansley Hotel, Atlanta, May 23-25, under the presidency of William H. Weir, Atlanta. Among the speakers were:

- John C. Dixon, Chicago, Rosenwald Fund, A Layman Looks at the Health Problems of Rural Georgia.
- William W. Cort, Ph.D., Baltimore, Johns Hopkins School of Hygiene and Public Health, Newer Knowledge About Hookworms and Hookworm Disease.
- Dr. Eugene L. Bishop, Chattanooga, director of health, Tennessee Valley Authority, Some Health Implications of Regional Water Control.
- Dr. William W. Bauer, Chicago, American Medical Association, Healthier Health Meetings.
- Dr. Joseph W. Mountin, Washington, D. C., Public Health Administration.

Dr. John R. Evans, Decatur, health commissioner of DeKalb County, was elected president of the association.

IDAHO

Postgraduate Lectures.—The state division of public health sponsored its third annual postgraduate lecture tour in April. Meetings were held at Idaho Falls, Twin Falls, Boise, Lewiston and Coeur d'Alene. The speakers were members of the faculty of the University of Oregon Medical School, Portland: Drs. Howard C. Stearns, Morris L. Bridgeman and Joyle Dahl.

ILLINOIS

Care for the Medically Indigent.—If a person becomes sick in Illinois and is unable to pay for necessary medical care, although otherwise self supporting, the county of residence may be required to compensate the attending physician for such services as have been previously authorized by the supervisor of the poor. To this effect was a recent decision of the Appellate Court of Illinois, fourth district, in the case of *Buckmaster et al. v. Effingham County*, 23 N. E. (2d) 747, 302 Ill. App. 353. The appellants in this case, a group of physicians, after being duly authorized, treated the minor child of a day laborer who was financially able to provide his family with all the necessities of life other than medical care. The court held that under the Illinois law the county must pay for the services rendered by these physicians.

Chicago

Personal.—Dr. Ludvig Hektoen, professor emeritus of pathology, University of Chicago School of Medicine and Rush Medical College, was awarded the honorary degree of doctor of science by the university, June 11, "in recognition of his scholarly achievements in basic science and his distinguished service to the university and to medicine as a great teacher, editor and administrator." Dr. Hektoen since 1937 has been executive director of the National Advisory Cancer Council of the U. S. Public Health Service.

Annual Prize of Chicago Surgical Society.—The second annual prize of \$250 of the Chicago Surgical Society was given to Dr. Leon J. Aries for a paper entitled "Experimental Analysis of the Growth Pattern and Rates of Appositional and Longitudinal Growth in the Rat Femur" and Dr. Carl Ireneus Jr. for a paper on "Experimental Bile Pancreatitis with Special Reference to Regeneration (Recovery) and to the Toxicity of the Hemorrhagic Exudate." The papers were presented at the meeting of the society May 10. Dr. Aries graduated at the University of Illinois College of Medicine, Chicago, in 1932, and Dr. Ireneus at the University of Illinois College of Medicine in 1936.

KENTUCKY

Annual Section Meeting.—The Eye, Ear, Nose and Throat Section of the Kentucky State Medical Association, which convenes separately from the association, met in Louisville, May 10. Dr. Albert C. Furstenberg, Ann Arbor, Mich., was the guest speaker on "Ménière's Disease." Other speakers included Drs. Roy Glenwood Spurling, on glossopharyngeal neuralgia; Melvin Clinton Baker, reflex neuralgia incident to disease conditions in the head; Adolph O. Phingst, cowpox infection of the eyes, and Joseph D. Heitger, management of nasal sinus disease. All are of Louisville.

Society News.—Lieut. Col. Edgar E. Hume, former librarian of the Army Medical Library, addressed the Innominate Society, Louisville, recently on "The Army Medical Library of Washington and Its Collection of Early Kentuckiana."—Drs. William T. McConnell and Granville S. Hanes addressed the Jefferson County Medical Society, Louisville, May 6, on "The Cervix and Its Relation to Childbirth" and "Diseases Affecting the Terminal Bowel" respectively.—Dr. Emmet F. Horine addressed the Louisville Medico-Chirurgical Society, May 24, on "Paroxysmal Tachycardia and Paroxysmal Auricular Fibrillation."

MASSACHUSETTS

Winner of Automobile at Annual Session.—Dr. William Parsons Boardman, professor of dermatology, Tufts College Medical School, Boston, was awarded a 1940 Oldsmobile four door sedan at the annual session of the American Medical Association June 10-14. Dr. Boardman held the lucky number in a drawing contest for which all Fellows registered at the convention were eligible.



MICHIGAN

Upper Peninsula Meeting.—The Upper Peninsula Medical Society will hold its annual meeting in Menominee, July 10-11. The session will open with a testimonial luncheon to officers of the state medical society with addresses by Drs. Burton R. Corbus, Grand Rapids, president, and Louis Fernald Foster, Bay City, secretary. Speakers on the scientific program will include:

Dr. Albert H. Montgomery, Chicago, Abdominal Conditions in Children.
Dr. Vincent J. O'Connor, Chicago, Recent Progress in Urology.
Dr. Rollin T. Woodruff, Chicago, Diabetes.
Dr. Lloyd E. Hamlin, Norway, Silicosis.
Dr. William L. Sherman, Detroit, Anuria.
Dr. LeMoyne Snyder, Lansing, Medicolegal Problems.
Dr. Elmer L. Sevrinhaus, Madison, Wis., Treatment of the Menopause.
Dr. Lemuel D. Smith, Milwaukee, Fractures of the Hip.

A luncheon and roundtable discussion on laboratory problems will conclude the meeting. At the annual banquet Wednesday evening, Dr. Rosco G. Leland, Chicago, will speak on "Health of the American People."

MINNESOTA

Annual Meeting of Radiologists.—Dr. Harry M. Weber, Rochester, was elected president of the Minnesota Radiological Society at its twelfth annual meeting in Rochester recently; other officers are Drs. Gustav T. Nordin, Minneapolis, vice president, and John P. Medelhan, St. Paul, secretary-treasurer. The annual Carman Lecture, sponsored by the society, was presented before the Minnesota State Medical Association during its annual meeting by Dr. Bernard H. Nichols, Cleveland, on "Indications for the Use of Excretory Urography in Diagnosis." At the dinner meeting of the radiological society Dr. Nichols spoke on "The Future of Radiology."

MISSOURI

State Medical Election.—Dr. Robert B. Denny, Creve Coeur, was named president-elect of the Missouri State Medical Association at its annual meeting in Joplin, May 1, and Dr. Cyrus E. Burford, St. Louis, was installed as president. Mr. Elmer H. Bartelsmeyer, St. Louis, is the executive secretary. The next annual session will be in St. Louis.

Beaumont the Soldier.—The Lloyd R. Bontwell Post number 136, American Legion, made up of physicians and dentists, held services, May 30, at the grave of Dr. William Beaumont, St. Louis. William R. Gentry, a St. Louis attorney,

gave the principal address entitled "Beaumont the Soldier." Dr. Beaumont was surgeon in the medical corps of the U. S. Army from 1812 to 1840 and a veteran of the war of 1812 and the Indian wars of 1827-1832.

Society News.—The Kansas City Society of Obstetrics and Gynecology was addressed, May 9, by Drs. Dwight T. Van Del on "Use of Testosterone Propionate in the Suppression of Lactation"; Harry B. Levey, "Delivery of a Primipara with Congenital Absence of the Rectum," and LeRoy Goodman, "Effect of Estrogenic Substances on Adenomyosis of the Uterus."—The Jackson County Medical Society was addressed, May 28, by Drs. William W. Buckingham and Victor B. Buhler, Kansas City, on "Pitfalls in the Diagnosis of Tuberculosis."—Dr. Theodore H. Saferstein discussed "Hypothyroidism" before the Buchanan County Medical Society in St. Joseph, May 8.—Dr. Robert L. Sanders, Memphis, Tenn., discussed problems of peptic ulcer before the Kansas City Surgical Society, May 23.

NEW JERSEY

State Medical Election.—Dr. Watson B. Morris, Springfield, became president of the Medical Society of New Jersey at the annual meeting in Atlantic City, June 4-6, and Dr. Thomas K. Lewis, Camden, president-elect. Dr. Elias J. Marsh, Paterson, was elected first vice president and Dr. Ralph K. Hollinshead, Westville, second vice president.

NEW YORK

Society News.—Drs. Albert Vander Veer and William J. Milner addressed the Medical Society of the County of Albany June 19, on "Traumatic Asphyxia" and "Modern Methods of Handling Prostatic Obstruction" respectively.—Dr. Harvey J. Matthews, Brooklyn, addressed the recent quarterly meeting of the Suffolk County Medical Society in Smithtown on "Obstet Shock."

Industrial Physicians Honor Dr. Gardner.—The American Association of Industrial Physicians and Surgeons, during its annual meeting in New York, June 6, presented the annual William S. Knudsen Award for outstanding achievement in industrial medicine to Dr. Leroy U. Gardner, director of the Saranac Laboratory for the Study of Tuberculosis, Saranac Lake, because of advances in the knowledge of silicosis resulting from research directed by him. Born in New Britain, Conn., Dr. Gardner received his medical degree at Yale University School of Medicine, New Haven, in 1914. Following a period of graduate study Dr. Gardner joined the faculty of Harvard Medical School in 1915, returning to his alma mater in 1917. He was pathologist to the Trudeau Foundation at Saranac Lake from 1918 to 1926, when he became director of the Saranac Laboratory for the Study of Tuberculosis. Since 1936 he has also been director of laboratories of the Trudeau Foundation.

New York City

Personal.—Dr. Fred H. Albee received the honorary degree of doctor of science at the annual commencement exercises of Rutgers University, New Brunswick, N. J., in recognition of his work in the fields of surgery and rehabilitation.—The alumni association of the De Lamar Institute of Public Health of Columbia University gave a dinner, May 2, in honor of Dr. Haven Emerson, whose approaching retirement as head of the institute was recently announced.—Drs. John M. Converse, New York, and Edgar A. Kahn, Ann Arbor, Mich., left during the week of June 10 for service with the American Hospital at Neuilly, near Paris.

Leslie Dana Gold Medal Awarded.—John M. Glenn, LL.D., New York, honorary vice president of the National Society for the Prevention of Blindness, was presented with the Leslie Dana Gold Medal, June 11, at the annual meeting of the Association for Research in Ophthalmology in New York. Mr. Glenn was selected by the St. Louis Society for the Blind through which the medal is offered by Mr. Leslie Dana of St. Louis. The medal is given on the recommendation of the research association for outstanding achievements in the prevention of blindness and the conservation of vision. Mr. Glenn has been identified with the organized movement for the protection of eyesight in America since its beginning in 1908. He was admitted to the bar in 1882. From 1898 to 1907 he was a member of the board of supervisors, Baltimore City Charities, serving as president from 1904 to 1907. From 1907 to 1931 he was general director of the Russell Sage Foundation.

Museum of Health Elects Officers.—Officers for the American Museum of Health, which is to be established as a permanent museum with certain exhibits now in the Medicine and Public Health Building at the World's Fair as a museum, were recently elected. Mr. George McAueny, chairman of the

board of the Title Guarantee and Trust Company, was made president and Mr. Frederick Osborn, a director of numerous corporations and trustee of various institutions, vice president. Louis I. Dublin, Ph.D., vice president of the Metropolitan Life Insurance Company, became chairman of the board of directors and Mr. Homer N. Calver, formerly secretary of the American Public Health Association, was elected secretary. Dr. Victor G. Heiser was elected to the board of directors. The museum of health sponsored a number of exhibits in the medical building at the fair in 1939 and again this year. According to the announcement, Mayor La Guardia has promised to make available a building for the permanent museum. Plans of the museum call for a broad program of health education, it was said. These include traveling exhibits to rural communities and exhibits for the use of schools, colleges, official and voluntary medical and health agencies and other organizations.

NORTH CAROLINA

State Medical Election.—Dr. Franklin Webb Griffith, Asheville, was named president-elect of the Medical Society of the State of North Carolina at its recent meeting in Pinehurst and Dr. Hubert B. Haywood, Raleigh, was installed as president. The 1940 session will again be held in Pinehurst.

Twenty-Five Years with Health Department.—Dr. George M. Cooper, assistant state health officer and director of the division of preventive medicine and health education in the state department of health, Raleigh, was given a silver inkstand as a memento by his associates, May 1, to mark his twenty-fifth anniversary with the department. Dr. Cooper began his work as director of rural sanitation, now called county health work, and later directed school health work for several years. He was made assistant state health officer in 1923. At various times he has also directed maternal and child health services and has acted as state health officer.

NORTH DAKOTA

State Medical Election.—Dr. Frederick W. Ferguson, Kulm, was chosen president of the North Dakota State Medical Association at the annual meeting in Minot, May 6, and Dr. Cyril J. Glaspel, Grafton, was installed as president. Drs. Alfred R. Sorenson, Minot, and Frank I. Darrow, Fargo, were elected vice presidents and Dr. Leonard W. Larson, Bismarck, secretary.

OREGON

Personal.—Dr. Courtney M. Smith, recently assistant health officer of Portland, has been appointed director of maternal and child health for Alaska.—Dr. Roy A. Payne, Portland, has been appointed to the state board of health to succeed Dr. Robert L. Benson, Portland.

Southern Oregon Meeting.—The annual meeting of the Southern Oregon Medical Society was held in Ashland, May 14, with the following speakers, all of Portland: Drs. Banner R. Brooke, "Examination, Diagnosis and Treatment of the Diarrheas"; Lyle B. Kingery, "Diagnostic Value of Certain Cutaneous Symptoms"; Noble Wiley Jones, "The Problem of Atherosclerosis and Atherosclerotic Heart Disease"; and Eugene W. Rockey, "Biliary Tract Surgery." In addition, Dr. Charles E. Hunt, Eugene, president of the Oregon State Medical Society, addressed the meeting.

PENNSYLVANIA

Society News.—Dr. Oscar V. Batson, Philadelphia, addressed the Dauphin County Medical Society, Harrisburg, June 4, on "Speech and Hearing Defects."—Drs. George Crile Jr. and Ernest P. McCullagh, Cleveland, were guests at the annual spring clinic of the Lycoming County Medical Society, Williamsport, June 7, conducting clinics and speaking on "Diagnostic and Surgical Aspects of Jaundice" and "Clinical Values of Testicular Hormones" respectively.—At a meeting of the Westmoreland County Medical Society, New Kensington, June 18, the speakers were Drs. Robert C. Grauer, Pittsburgh, on "Mediastinal Parathyroid Adenoma with Recovery"; William T. Holland, Springdale, "Present Status in the Treatment of Pneumonia," and Charles L. Hobaugh, New Kensington, "A Case of Papillary Cyst Adenoma."

Philadelphia

Dr. Tracy Honored.—Dr. Martha Tracy, assistant director of public health of Philadelphia and retiring dean of the Woman's Medical College of Pennsylvania, was honored at a dinner recently. The speakers included Mayor Lambertson; Dr. Hubley R. Owen, director of public health; Marion Edwards Park, LL.D., president of Bryn Mawr College;

Drs. William Pepper and William N. Parkinson, deans, respectively, of the medical schools of the University of Pennsylvania and Temple University. Dr. Tracy took her medical degree from the Woman's Medical College of Pennsylvania in 1904 and the degree of doctor of public hygiene from the University of Pennsylvania in 1917. She has been associated with the woman's college since 1913, as professor of physiologic chemistry, professor of hygiene, professor of preventive medicine and since 1918 dean. Early this year Dr. Tracy was appointed assistant director of public health of Philadelphia but continued her duties as dean until the end of the college year.

Society News.—At a meeting of the Obstetrical Society of Philadelphia recently the speakers were Drs. Bernard Mann, David R. Meranze and Benjamin Leff on "Ovarian Pregnancy" and Henry D. Lafferty, "Sudden Death During or Immediately Following Labor."—Speakers before the Philadelphia Laryngological Society, April 2, were Comdr. Travis S. Moring, U. S. Naval Hospital, Philadelphia, on "Treatment of Purulent Maxillary Sinusitis"; Lieut. Comdr. Clifford A. Swanson, U. S. Naval Dispensary, Washington, D. C., "Roentgen Ray Therapy of Acute Otitis and Acute Mastoiditis," and Rear Admiral Ross T. McIntire, surgeon general, U. S. Navy, "Problems that the Specialist in Otolaryngology Meets in the Navy."

Pittsburgh

Cancer Meeting for the Public.—A public meeting on cancer was arranged by the Allegheny County Medical Society, the state department of health and the Homewood-Brushton Community Council, May 28. The program of addresses was followed by a forum with questions from the audience. The speakers were:

Dr. Albert J. Bruecken, What You Should Know About Cancer.
Dr. William A. Wycoff, Cancer of the Stomach or Intestinal Tract.
Dr. Edwin P. Buchanan, Cancer of the Breast.
Dr. Lester Hollander, Cancer of the Skin and Mouth.

UTAH

Personal.—Dr. Mancel T. Mitchell, Eau Claire, Wis., has accepted a position as obstetric consultant to the division of maternal and child health in the Utah State Board of Health, Salt Lake City.

Society News.—The Carbon County Medical Society was addressed in Price, May 12, by Drs. Edward L. Van Aelstyn, Price, on streptococcal sore throat, and Dr. Frank V. Colombo, Price, "The Catabolism of Hemoglobin."—Dr. Edward C. Rosenow, Rochester, Minn., discussed "Experimental Studies on the Etiology of Influenza and Persistent Epidemic and Post-operative Hiccup" at a joint meeting of the Salt Lake, Weber and Utah county medical societies in Salt Lake City, May 3.

WISCONSIN

Personal.—Dr. Henry V. Bancroft, Blue Mounds, was honored with a scroll of appreciation by the Dane County Medical Society at a meeting in Madison, May 20. Dr. Bancroft, who is 80 years old, has been a member of the society for fifty-five years. Dr. Frank H. Lahey, Boston, was the speaker of the evening.—Dr. Carl W. Eberbach, Milwaukee, has been appointed to the state board of health to succeed Dr. John J. Seelman, Milwaukee. His term will expire in February 1947.

Marquette Alumni Meeting.—The Marquette University School of Medicine Alumni Association presented an all-day clinic program at the school in Milwaukee, May 8. Dr. James P. Simonds, Chicago, was the speaker at a banquet in the evening on "The General Practitioner and Modern Medicine." Among the speakers on the day program were:

Dr. Armand J. Quiek, Advances in Knowledge of Treatment of Hemorrhage.
Dr. Harry Beekman, Development of New Chemotherapeutic Agents.
Dr. David A. Cleveland, Surgery of the Sympathetic Nervous System.
Dr. Ronald S. Cron, Clinical Use of Female Sex Hormones.
Dr. Francis D. Murphy, Use of Sulfanilamide and Allied Compounds in Clinical Medicine.

Society News.—Dr. Alexander E. Brown, Rochester, Minn., addressed the Medical Society of Milwaukee County, Milwaukee, May 10, on "Sulfapyridine and New Compounds."—Drs. Edward R. Krumbiegel, Milwaukee, and Edward T. Evans, Minneapolis, addressed the Chippewa County Medical Society, May 21, in Chippewa Falls on "Acute Communicable Diseases—Their Diagnosis and Management" and "Common Sense in the Treatment of Fractures" respectively.—Drs. Robert B. Malcolm, Chicago, and Millard Tufts, Milwaukee, addressed a joint meeting of the Racine, Walworth and Kenosha county medical societies in Racine, May 16, on "Tumors of the Neck" and "Clinical Aspects of Electrocardiography" respectively.—

Dr. Frederick W. Madison, Milwaukee, discussed arthritis at a meeting of the Fond du Lac County Medical Society, Fond du Lac, May 28.—Dr. Paul C. Bucy, Chicago, addressed the La Crosse County Medical Society, La Crosse, May 7, on "Early Signs and Symptoms of Brain Tumor" and "Infectious Complications Following Swimming" respectively.—Dr. Theodore L. Squier, Milwaukee, discussed allergy at a meeting of the Eau Claire-Dunn-Pepin Counties Medical Society, Eau Claire, May 27.

GENERAL

Examination in Neurologic Surgery.—The American Board of Neurological Surgery will hold its first examination to certify candidates at the University of Illinois, 804 South Wood Street, Chicago, October 18-19. Application forms and copies of the charter and by-laws may be obtained from the secretary, Dr. Roy Glenwood Spurling, 404 Brown Building, Louisville, Ky.

P. P. Jacobs Dies.—Philip P. Jacobs, Ph.D., Morristown, N. J., for many years associated with the National Tuberculosis Association, died at his home June 12 after an illness of three months, aged 61. Dr. Jacobs became assistant secretary of the tuberculosis association in 1908 and for many years had been director of personnel training and publications. He had conducted institutes for the training of tuberculosis and health workers throughout the United States since 1917. He was the author of "The Campaign Against Tuberculosis in the United States" and "The Control of Tuberculosis in the United States." In 1924 he was decorated by the Danish government in recognition of his work.

Dr. Swain Awarded Remington Medal.—Robert L. Swain, Pharm.D., New York, who recently concluded twenty years as secretary-treasurer of the Maryland Board of Pharmacy, has been awarded the Remington Medal by the New York branch of the American Pharmaceutical Association. Dr. Swain has served as chairman of the Conference of Law Enforcement Officials; president of the American Pharmaceutical Association and the National Association of Boards of Pharmacy; editor of *Drug Topics*, and deputy commissioner of food and drugs for Maryland. The medal was awarded for Dr. Swain's contributions toward uniformity and modernization of legislation governing the practice of pharmacy. It will be presented at a dinner, the date of which has not yet been announced.

Fellowships in Child Psychiatry Available.—The National Committee for Mental Hygiene announces that a limited number of fellowships have been provided by the Commonwealth Fund and other sources for training in extramural psychiatry, especially child psychiatry. The committee is to assign fellows for one or two years at a selected child guidance clinic, the term and plan of the fellowship to be determined by the needs of each fellow. Candidates for these awards should have had at least two years of psychiatry in an approved mental hospital in addition to other qualities fitting them for extramural service. These fellowships come in response to a definite paucity of personnel in this field, it was said. Accordingly, other conditions as to age, sex and marital status must be governed by individual cases and by current demand, according to the announcement. Requests for further information should be addressed to Dr. Milton E. Kirkpatrick, National Committee for Mental Hygiene, Room 822, 50 West Fiftieth Street, New York.

Special Society Elections.—Dr. Esmond R. Long, Philadelphia, was chosen president of the American Association of the History of Medicine at its annual meeting, May 1, and Dr. Henry E. Sigerist, Baltimore, was reelected secretary. The next annual session will be held at Atlantic City, N. J., May 4-6, 1941. The association also plans to hold a fall meeting in Cleveland October 7 this year under the auspices of the Ohio Committee for Medical History and Archives, with Dr. Howard Dittrick, Cleveland, as chairman.—The new officers of the American Neurological Association include Drs. Harold Douglas Singer, Chicago, president; Harry C. Solomon and Gilbert Horrax, Boston, vice presidents.—Dr. Theodore Riley, New York, was reelected secretary.—Dr. Theodore Lyle Hazlett, Pittsburgh, was chosen president-elect of the American Association of Industrial Physicians and Surgeons at its annual session in New York, June 7, and Dr. Daniel L. Lynch, Boston, was installed as president. Drs. John J. Wittmer, New York, and John J. Prendergast Jr., Detroit, were made vice presidents.—Dr. William B. Castle, Boston, was elected president of the American Society for Clinical Investigation at its recent annual session. Dr. Eugene M. Landis, Charlottesville, Va., is secretary. The next annual session will

be held in Atlantic City, N. J., May 5, 1941.—Dr. Thomas B. Cooley, Detroit, was named president of the American Pediatric Society at its annual session in May. Dr. Hugh McCulloch, St. Louis, is secretary.

Pacific Northwest Medical Association.—The annual meeting of the Pacific Northwest Medical Association will be held at the Davenport Hotel, Spokane, July 10-13, under the presidency of Dr. Charles E. Sears, Portland, Ore. Guest speakers will include:

Dr. Wilder G. Penfield, professor of neurology and neurosurgery, McGill University Faculty of Medicine, Montreal.

Dr. Frederick A. Celler, professor of surgery, University of Michigan Medical School, Ann Arbor.

Dr. Henry G. Pancher, associate professor of pediatrics, University of Illinois College of Medicine, Chicago.

Dr. Andrew B. Stockton, assistant clinical professor of medicine, Stanford University School of Medicine, San Francisco.

Dr. John S. Lundy, department of anesthesia, Mayo Clinic, Rochester, Minn.

Dr. Anton J. Carlson, Frank P. Hixon distinguished service professor of physiology, Division of Biological Sciences, University of Chicago.

Dr. Richard W. Telford, professor of gynecology, Johns Hopkins University School of Medicine, Baltimore.

Dr. Fred H. Kruse, clinical professor of medicine, University of California Medical School, San Francisco.

Dr. William Edward Chamberlain, professor of radiology and roentgenology, Temple University School of Medicine, Philadelphia.

Dr. Harold E. Robertson, pathologist at the Mayo Clinic, Rochester, Minn.

CORRECTION

First State Owned Cancer Hospital.—In a news item in THE JOURNAL, June 15, page 2393, appears the statement that the state cancer hospital of Columbia, Mo., opened April 26, "is said to be the 'first hospital ever established by a state for the exclusive care of cancer sufferers.'" The commissioner of public health of Massachusetts writes that a state cancer hospital, the Pondville Hospital, authorized by the Massachusetts legislature, was opened June 23, 1927. It has been operated continuously since that time by the Massachusetts Department of Public Health and has always been restricted exclusively to cancer patients. The present capacity of the hospital is 145 beds.

Government Services

Nurses Wanted in Panama Canal Service

The U. S. Civil Service Commission announces an open competitive examination to fill graduate nurse positions in the Panama Canal Service for general staff duty and psychiatric duty. The entrance salary is \$168.75 a month, subject to a retirement deduction of 5 per cent and a deduction of \$40 a month for subsistence and quarters. Applications must be filed with the commission's Washington office not later than July 22 if received from states east of Colorado; not later than July 25, if received from Colorado and states westward, and not later than August 26 if received from the Panama Canal Zone. Full information and the necessary application forms may be obtained from the secretary of the Board of U. S. Civil Service Examiners at any first or second class postoffice or from the U. S. Civil Service Commission, Washington, D. C.

Collection on Gastronomy Given to Library of Congress

A collection of books on gastronomy has been given to the Library of Congress, Washington, D. C., by Dr. Arvill W. Bitting, food technologist of San Francisco, in memory of his wife, Katherine Golden Bitting, who died in 1937. The collection was assembled during their lifelong investigations into the chemistry, bacteriology and history of foods. The Library of Congress has agreed, as an exception to its usual procedure, to establish the Katherine Golden Bitting Collection on Gastronomy as a separate unit among its collections, where it may be readily available, in conjunction with her bibliography, to present and future students in the field to which she so fruitfully dedicated her life, according to an announcement Mrs. Bitting graduated at Purdue University, remaining there as an instructor and assistant professor in botany and biology; in 1904 she married Dr. Bitting, her lifelong collaborator in her work on foodstuffs, also at that time a member of the Purdue faculty. In 1907 both joined the staff of the bureau of chemistry of the U. S. Department of Agriculture.

Foreign Letters

LONDON

(From Our Regular Correspondent)

May 25, 1940.

Reduction of Sugar and Butter Rations

A partial failure of the sugar crop in the British West Indies and the necessity for conserving current resources have rendered necessary a reduction in the weekly sugar ration from 12 to 8 ounces. Glucose also will be rationed. The loss of Denmark and Holland as sources of butter has rendered necessary a reduction of the weekly butter ration from 8 to 4 ounces. It is also expected that the bacon ration, now 8 ounces, will soon have to be cut.

Mobile X-Ray Unit for the Army

Miss Iris Michaelis, daughter of the South African philanthropist, has presented to the British army in memory of her father a mobile x-ray unit for service at the front. It is mounted on a standard lorry chassis and electric current is obtained from a gasoline driven generator packed underneath the unit when not in use. Thus it can operate in places where there is no electrical supply. The unit also carries its own water supply in a tank underneath the vehicle, and a jack is provided to maintain absolute steadiness when at work. The interior is air conditioned and shock proof throughout. It is divided into two compartments, the larger being fitted as an x-ray operating room with a full size table, movable x-ray tube and screening stand. The other compartment can be quickly converted into a dark room. The unit was designed by Lieut.-Col. D. B. McGrigor, assisted by the manufacturers, Watson and Sons.

The Prevention and Treatment of Tetanus in the War

For the prevention and treatment of tetanus in the British army, both passive and active immunization are in use for every man. Passive immunization is produced by injecting a prophylactic dose of antitoxin as soon as possible after the man has been wounded, active immunization by two injections of formol toxoid sometime before going on active service. The value of passive immunization was shown in the last war. The few who developed the disease after a prophylactic injection usually had a long incubation period and slow onset and recovered. The disadvantages of this treatment are that the injection has to be given soon after the wound is received; in some cases it has to be repeated and serum reactions are liable to occur. Active immunization has the advantages that it can be produced before the soldier goes on active service and that the immunization probably lasts many years. But it has not yet been tested on a large scale in war. The only disadvantage is slight allergic reactions, which are attributed to a small amount of peptone present.

In an address to a medical society of the British Expeditionary Force Lieut.-Col. L. B. Cole, an authority on tetanus, recommended that antitoxin be injected intravenously as soon as possible after the man is wounded. He recommended 200,000 units as large enough to neutralize all unfixed toxin and prevent further absorption. There was no advantage in repeating the dose except in the case of severe infected wounds, when an additional 50,000 units might be given intramuscularly once a week. For control of the spasms he recommended avertin with amylene hydrate by rectum as for basal anesthesia. In severe cases this would stop the convulsion in from four to six hours, when it had to be repeated. In some cases two or three such doses daily for eight or more days might be necessary. An alternative to avertin with amylene hydrate was rectal paraldehyde in basal anesthetic doses.

Foreign Synthetic Drugs

In peace times we imported from Germany the majority of synthetic drugs. On the outbreak of war the Medical Research Council took steps, in conjunction with governmental departments and the Association of British Chemical Manufacturers, to secure that we shall not be without the important synthetic drugs hitherto obtained from abroad. Some of the British substitutes can have their identity proved by chemical means, but for others the council has thought clinical trials necessary to insure that they are equivalent in all respects to proprietary products hitherto imported under trade names. The result is that chemical names now take the place of trade names. Thus avertin has become bromethol; evipan sodium, soluble hexobarbitone. The General Medical Council will publish as an addendum to the last edition of the British Pharmacopeia, which was published in 1932, articles dealing with other foreign drugs which are now being produced or are likely soon to be produced by British manufacturers. Hitherto these have been known under registered trade names, but they will now be given official pharmacopeial names.

STOCKHOLM

(From a Special Correspondent)

April 9, 1940.

(This letter, mailed April 9 from Bergen, Norway, arrived on June 24 after passing through the German censorship, apparently by way of Salonika, Greece.)

The Fitness of Swedish Doctors for Army Service

Recent events have stressed the need for a fully documented card index of the doctors and medical students with reference to their fitness for army medical service in case of war. In October 1939 the medical societies throughout Sweden agreed to the compiling of such a card index to cover the Universities of Stockholm, Uppsala and Lund. The information collected in this index concerned, among other things, a summary of the physical condition of each doctor and medical student and the opinions of the doctors themselves as to their ability to serve in the field or undertake exacting duties in the hospital. This index sheds a most disquieting light on the high frequency of tuberculosis in the medical profession; it was far and away the most important cause of faulty health disqualifying for military service. Indeed, between 43 and 44 per cent of all the exemptions from military service were based on tuberculosis. Some form or other of heart disease came next in the list of disqualifications, but these cases were only half as numerous as those of tuberculosis. Altogether only 71 per cent of all the doctors could be considered as fit for military service. In other words, in the event of war 11 per cent of the doctors could not be called up for army service because they were women and 18 per cent because they were not fit enough. The tuberculosis rate was somewhat lower among the medical students than among the doctors, presumably because exposure to infection had not been so long on the average for the students and because there has been a marked decline in the incidence of tuberculosis in the past generation.

The Evolution of Hospital Treatment for Children

At the last annual meeting of the Swedish Association of Pediatricians Prof. Curt Gyllenswärd of Stockholm delivered a statistically inspired lecture on the evolution of children's hospitals and the social work now being done in them. It is curious how rapid and fundamental has been the revolution in Swedish hospitals for children. A generation or two ago these hospitals catered mainly to severe cases of well defined disease, whereas they are now made use of more and more for acute cases which formerly would have been treated at home unless some operation had to be performed. It might well have been thought that with birth control and the dwindling numbers of children (there are now some 2,000 fewer children in Stock-

holm than there were only ten years ago) the claims on the beds in hospitals for children would have diminished. So far from this being the case, the claims on such beds have increased by 50 per cent in the last decade.

The Passing of the Maiden Aunt

Why is the sick child, formerly nursed at home, now bundled off to a hospital at short notice and kept there till all is well again? Professor Gyllenswärd finds the answer to this question in the modern home which the mother leaves to follow some employment elsewhere and which is now bereft of the unattached maiden aunt, not to mention the grandmother, who in former days used to be considered a superfluous nuisance but who in reality often proved the mainstay of the family. Acid and angular the maiden aunt may have been, but she was more than worth her salt in the countless emergencies of a large family. Another inducement for parents to send their sick children to hospitals in Stockholm is the modesty of the charges made for their accommodation—only 2.50 kronor (60 cents) a day. Thus for a *fortnight's treatment* the parents have to pay only 35 kronor (\$8.35) and, as a matter of fact, only 46 per cent of the children are paid for at this rate, some reduction or complete exemption being obtained for the remainder. Professor Gyllenswärd pleaded urgently for a more comprehensive and sympathetic study of the hospital child's spiritual and mental needs than has heretofore been devoted to him.

Aid for Swedish Doctors in Finland

Several members of the Swedish Medical Association have undertaken to contribute the earnings of one day a month to aid for Finland. This association has established a guaranty fund of 660,000 kronor (\$157,608) for the support of the dependents of those doctors who have gone to Finland, in the event of their being killed or wounded.

• BUENOS AIRES

(From Our Regular Correspondent)

May 24, 1940.

Cancerigenic Factors

Prof. Angel H. Roffo of Buenos Aires recently demonstrated that cholesterol contained in the body and in foods such as meat, fats and eggs, when activated by the ultraviolet rays of the sun, produces fluorescent and radioactive hydrocarbons of a cancerigenic character. He further called attention to his belief that the increase in the large cities of carcinoma of the respiratory organs was due to exhaust gas of motor vehicles. He was able to extract from the air of one of the busiest streets of Buenos Aires relatively large quantities of a mineral oil the absorption lines of which were contained within the same angstrom units and showed the same qualities of fluorescence as the oil which was obtainable from cotton filters placed in the pipes by which carburetors are fed. Certain quantities of mineral oil containing polycyclic hydrogens are found in the air, derived, no doubt, from the incomplete combustion not only of motors that use benzene but of Diesel motors as well. Roffo has also shown in rat experimentation that carcinoma of the lungs develops if rats are compelled to live for several months in an atmosphere contaminated by Diesel oil combustion products.

Public Health Administration in Chile

A new division concerned with the connection between nutrition and health has been created in Chile's department of public health with authority to investigate the nutritional status of the whole country. It exercises control over milk and veterinary inspection and over foods, diets, educational campaigns and laboratories. Special legal enactments are being planned with relation to the manufacture and sale of margarine and smoked fish, milk and milk products, horse meat and vinegar.

At certain times in which milk production went through a crisis this branch of the health service established centers for the rationing of milk. This kept the price of milk down. At the same time an extensive campaign was conducted showing the highly nutritious value of milk. Milk served to school children will soon reach 23 per cent of such children. Breakfasts furnished to school children at present contain 271 calories.

The commission for the control of the price of drugs in general, existing since 1932, has not been able to function properly in the past. Prices and detailed specifications have now been set up for more than 2,000 medicinal products, thereby not only preventing speculation in drugs but enabling the public to obtain medicaments at a lower price than can be obtained in other countries.

A special division for the control of venereal diseases has been created in which the different health boards, the army and scientific societies are cooperating. There is no charge for treatments. These are compulsory only for the army. It is planned to place all venereal diseases under the control of the department of preventive medicine and to organize prophylactic centers in the large industries. Sex education should, it is believed, begin early, in cooperation with schools and churches. The division for venereal diseases favors the abolition of legalized prostitution.

Rabies in Argentina and Cuba

Central headquarters for rabies control in Argentina is the Instituto Antirrábico Pasteur in Buenos Aires, under the direction of Dr. Carlos Ramos Mejía. This is a municipal institute but cooperates with the National Department of Public Health, since its activities embrace the whole country. Founded in 1886, it has grown during the last two decades. In the half century intervening between 1886 and 1937 about 200,000 persons were observed, 70,000 of whom were treated. The average mortality was 3 per thousand. In 1937 more than 13,000 dogs were examined and positive infections found in about 240. By charting the possible entries by which rabid animals made their way into the city, it was found that two villages especially were responsible for rabic infection.

In Cuba, according to recent data, more than 32,000 dogs were inoculated against rabies in 1936-1937. Positive reactions were obtained in only seven of ninety-seven suspected dogs. In Cuba dead vaccines were used, which excludes the possibility of creating carriers through vaccination. Inoculation of dogs at the expense of the owner is now being required in Cuba.

Marriages

EUGENE S. HOPPENSTEIN, San Francisco, to Miss Isabel M. Armstrong of Lewiston, Idaho, in Seattle, April 3.

PHILLIP H. HALPERIN, Madison, Wis., to Miss Dorothy Milgram of Kansas City, Mo., April 9.

AUGUSTINE NOVELLO, Ashtabula, Ohio, to Miss Eleanor Eileen Finnerty of Cleveland in April.

CLAUDE C. NUCKOLS JR. to Miss Margaret Weatherwax, both of Albany, N. Y., April 20.

CHARLES J. AUCREMAN, Montpelier, Ind., to Miss Marcella Gillum of Winchester, June 6.

J. ZEB McDANIEL to Miss Opal Lois Dowden, both of Augusta, Ga., April 13.

WILLIAM J. MAUERMANN, Beloit, Wis., to Miss Lois Alton of Madison, April 2.

EUGENE B. LEY to Miss Marie Barbara Cabar, both of Detroit, June 17.

EUGENE C. SMITH to Miss Helene Sullivan, both of Flint, Mich., May 7.

VIOLET H. KIDD, Souderton, Pa., to Rev. Paul M. Scholl recently.

Deaths

John Taylor Fotheringham, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1891; Trinity Medical College, Toronto, 1891; emeritus professor of the history of medicine at the University of Toronto Faculty of Medicine; fellow of the American College of Surgeons and the American College of Physicians; was assistant director of medical service of the Second Canadian Division in France and director-general of medical service in Canada during the World War; consultant, Hospital for Sick Children and Toronto General Hospital; aged 79; died, May 9.

John Glover South, Louisville, Ky.; University of Louisville (Ky.) Medical Department, 1897; member and past president of the Kentucky State Medical Association; director of the bureau of registration and past president of the state board of health; member of the House of Delegates of the American Medical Association in 1920-1921; formerly United States Minister to Panama and Portugal; at one time health officer of Franklin County; aged 67; died, May 13.

John Herman Wylie, Peiping, China; Columbia University College of Physicians and Surgeons, New York, 1912; a medical missionary for the Board of Foreign Missions of the Presbyterian Church of the United States of America; on the staff of the Douw Hospital; aged 55; died, May 7, in a hospital at Cleveland following an operation for brain tumor.

Emil Alexius Edlen, Moline, Ill.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1892; member of the Illinois State Medical Society; at one time city physician; aged 80; formerly on the staffs of the Moline Public Hospital and the Lutheran Hospital, where he died, May 10, of uremia, myocarditis and arteriosclerosis.

Walter Scott Rountree, Birmingham, Ala.; Birmingham Medical College, 1900; member of the Medical Association of the State of Alabama; fellow of the American College of Surgeons; served during the World War; gynecologist to the Hillman Hospital; surgeon to the Norwood Hospital; aged 66; died, May 6, of cerebral hemorrhage.

Charles William Schmehl, Cleveland; University of Pennsylvania Department of Medicine, Philadelphia, 1893; member of the Medical Society of the State of Pennsylvania; past president and secretary of the Warren County Medical Society; at one time health officer of Warren, Pa.; aged 66; died, May 17, in a local hospital of pneumonia.

Wade MacMillan, Oxford, Ohio; Miami Medical College, Cincinnati, 1891; professor of orthopedic surgery at his alma mater from 1905 to 1907; for many years medical director of Miami University; aged 75; for many years surgeon to the Christ Hospital, Cincinnati, where he died, May 13, of cerebral arteriosclerosis and thrombosis.

Raymond Nazaire Filiatreau, Elwood, Ind.; Marion-Sims College of Medicine, St. Louis, 1899; University of Louisville (Ky.) Medical Department, 1900; member of the Indiana State Medical Association; served during the World War; aged 67; died, May 16, in the Mercy Hospital of pulmonary tuberculosis and diabetes mellitus.

Paul Emerson Gilmor, Canal Fulton, Ohio; Western Reserve University School of Medicine, Cleveland, 1916; formerly a medical missionary; formerly county health officer; aged 50; on the associate staff of the Massillon City Hospital, where he died, May 16, of coronary heart disease.

John H. Oliver, Kewanee, Ill.; Beaumont Hospital Medical College, St. Louis, 1896; past president of the Henry County Medical Society; on the staff of the Kewanee Public Hospital; aged 69; died, May 16, in the Evanston (Ill.) Hospital of coronary occlusion and arteriosclerosis.

John A. Devron, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1896; served during the Spanish-American and World wars; aged 66; died, May 13, at the Baptist Hospital of arteriosclerotic heart disease, diabetes mellitus and pneumonia.

Irving Wagner Metz, Springfield, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; member of the Illinois State Medical Society; aged 67; died, May 12, of cerebral hemorrhage, arteriosclerosis and hypertension.

Lyman Allen Steffen, Antigo, Wis.; Rush Medical College, Chicago, 1912; past president of the Langlade County Medical Society; served during the World War; city health officer; on the staff of the Langlade County Memorial Hospital; aged 52; died, April 10.

William Joseph Linley, Columbia, S. C.; Medical College of the State of South Carolina, Charleston, 1892; formerly associated with the United States Public Health Service; aged 69; died, May 1, in the Anderson County Hospital, Anderson, of cerebral hemorrhage.

Joseph Ambrose Cox, Albany, N. Y.; Albany Medical College, 1901; fellow of the American College of Surgeons; served during the World War; attending surgeon to St. Peter's and Brady Maternity hospitals, and Infant Home; aged 61; died, April 23.

Caleb A. Calvert, Scottsville, Ky.; Barnes Medical College, St. Louis, 1898; past president and secretary of the Allen County Medical Society; at one time county health officer; aged 63; died, May 26, of cerebral hemorrhage and arteriosclerosis.

Herman Albert Hanser, St. Louis; Missouri Medical College, St. Louis, 1898; fellow of the American College of Surgeons; for many years on the staff of the Lutheran Hospital; aged 62; died, May 28, in Flagstaff, Ariz., of heart disease.

John W. Craig, Chicago; College of Physicians and Surgeons, Keokuk, Iowa, 1881; an Affiliate Fellow of the American Medical Association; member of the Iowa State Medical Society; aged 83; died, May 6, of chronic myocarditis.

Benjamin Thomas Atkins, Charlotte, N. C.; Medical College of the State of South Carolina, Charleston, 1901; aged 62; died, May 9, in the Rowan Memorial Hospital, Salisbury, of urinary extravasation with gangrene and urethral stricture.

Benjamin Franklin Easter, New Orleans; Meharry Medical College, Nashville, Tenn., 1903; aged 65; died, May 16, in the Flint Goodridge Hospital of bronchopneumonia, following a vertebral fracture received in a fall.

Wilkins McDade, Minden, La.; Memphis (Tenn.) Hospital Medical College, 1909; past president and secretary of the Webster Parish Medical Society; aged 54; died, May 24, of injuries received in an automobile accident.

Pete Ernest Magoun, Vidalia, La.; University of Louisville (Ky.) Medical Department, 1906; member of the Louisiana State Medical Society; for many years parish coroner; aged 56; died, April 8, in a hospital at Natchez, Miss.

William Avery Gaylord, Pawtucket, R. I.; Harvard Medical School, Boston, 1899; member of the Rhode Island Medical Society; on the consulting staff of the Memorial Hospital; aged 65; died, May 22, of coronary thrombosis.

Richard Kring, St. Louis; Missonri Medical College, St. Louis, 1891; served during the World War; aged 76; died, May 16, in the Veterans Administration Facility, Danville, Ill., of chronic myocarditis and arteriosclerosis.

Charles Hamilton, Carlock, Ill.; College of Physicians and Surgeons, Chicago, 1895; on the staff of the Brokaw Hospital, Normal; aged 70; died, April 15, of bronchopneumonia, arteriosclerosis, cerebral thrombosis and uremia.

Benjamin Chase Grout, Berwyn, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; aged 69; died, May 12, of coronary occlusion and arteriosclerosis.

Preston Thompson, Lebanon, Mo.; Washington University School of Medicine, St. Louis, 1913; member of the Missouri State Medical Association; served during the World War; aged 51; died, April 14.

George Henry Bowles, Toronto, Ont., Canada; M.B., University of Toronto Faculty of Medicine, 1892; M.D., Victoria University Medical Department, Coburg, 1892; aged 76; died, April 10.

William Lee Patterson, El Dorado, Ark.; Memphis (Tenn.) Hospital Medical College, 1910; member of the Arkansas Medical Society; aged 60; died, May 29, of a self-inflicted bullet wound.

Samuel Victor King, Sharon, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1901; fellow of the American College of Surgeons; served during the World War; aged 63; died, April 3.

George Frederick Sneed, Kirksville, Mo.; St. Louis University School of Medicine, 1926; aged 47; died, May 10, in the Barnes Hospital, St. Louis, following an operation for brain tumor.

Foster Thomas Jones, New Orleans; Meharry Medical College, Nashville, Tenn., 1917; aged 50; on the staff of the Flint Goodridge Hospital, where he died, May 28, of cerebral hemorrhage.

Riley F. Cheatham, Diamond, Mo.; St. Louis College of Physicians and Surgeons, 1903; member of the Missouri State Medical Association; aged 70; died, April 3, of carcinoma of the prostate.

John Luther Pittman, Palmetto, La.; Memphis (Tenn.) Hospital Medical College, 1908; served during the World War; aged 72; died, April 19, in the Veterans Administration Facility, Alexandria.

James Ora Pearman, Mahomet, Ill.; Rush Medical College, Chicago, 1885; aged 80; died, May 4, in the Burnham City Hospital, Champaign, following an operation for prostatic obstruction.

Ernest Rowland @ Liberty Grove, Md.; Baltimore Medical College, 1895; past president of the Cecil County Medical Society; aged 65; died, April 27, of chronic myocarditis and nephritis.

Robert Yates Hayne Thomas, Jacksonville, Fla.; Medical College of the State of South Carolina, Charleston, 1904; member of the Florida Medical Association; aged 63; died, April 14.

Vasco Mortimer Beecher Jr., Atlanta, Ga.; Emory University School of Medicine, Atlanta, Ga., 1937; aged 25; died, May 21, at Marianna, Fla., of injuries received in an automobile accident.

David Thomas Muir, Alden, Kan.; University of Tennessee Medical Department, Nashville, 1901; member of the Kansas Medical Society; aged 70; died in May of carcinoma of the bladder.

Francis M. Reed, Turrell, Ark. (licensed in Arkansas in 1903); aged 69; died, May 6, in St. Joseph's Hospital, Memphis, Tenn., of leukemia, chronic nephritis and bronchopneumonia.

Arthur Eugene Knoefel Sr. @ Black Mountain, N. C.; University of Louisville (Ky.) Medical Department, 1893; town health officer; aged 67; died, May 20, of coronary occlusion.

Arthur Joseph Babin, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1896; aged 66; died, May 19, of chronic nephritis and cirrhosis of the liver.

John D. Ball, Lexington, Mo.; Melharry Medical College, Nashville, Tenn., 1892; aged 80; died, May 23, in St. Margaret's Hospital, Kansas City, Kan., of ascending pyelonephritis.

Louis Philippe Dorval, Montreal, Que., Canada; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1903; aged 60; died, April 24.

Arthur West Allen, Austin, Minn.; Rush Medical College, Chicago, 1885; member of the Minnesota State Medical Association; aged 77; died, May 6, of carcinoma of the sigmoid.

Charles H. Lockhart @ Witt, Ill.; Missouri Medical College, St. Louis, 1898; on the staff of St. Francis Hospital, Litchfield; aged 68; died, May 17, of cerebral hemorrhage.

George B. Smith, Toronto, Ont., Canada; M.B., University of Toronto Faculty of Medicine, 1880; M.D., Victoria University Medical Department, Coburg, 1880; aged 88; died, May 16.

William Robert Gilbert, Tyro, Miss.; Kentucky University Medical Department, Louisville, 1904; member of the Mississippi State Medical Association; aged 61; died, April 5.

Ney Milton Salter @ Williams, Calif.; Northwestern University Medical School, Chicago, 1911; county health officer; served during the World War; aged 55; died, April 13.

Frank Marvin Banker, Franklin Grove, Ill.; Rush Medical College, Chicago, 1892; for many years county coroner; aged 72; died, May 30, of myocarditis and diaphragmatic hernia.

John William Hayes, Franklin, Ky.; University of Louisville (Ky.) Medical Department, 1889; member of the Kentucky State Medical Association; aged 75; died, April 10.

William T. McDonald, Vilonia, Ark. (licensed in Arkansas in 1903); member of the Arkansas Medical Society; aged 74; died, May 26, of chronic myocarditis and nephritis.

Sydney Fredrick Tichborne, Toronto, Canada; Queen's University Faculty of Medicine, Kingston, Ont., 1918; served during the World War; aged 46; died, April 4.

Richard Allen, Winchester, Ky.; University of Louisville Medical Department, 1890; aged 81; died, May 30, in the Clark County Hospital of cerebral hemorrhage.

Joseph L. Barber, Marathon, Wis. (licensed in Wisconsin in 1925); member of the State Medical Society of Wisconsin; formerly state senator; aged 76; died, April 6.

Harold Austin Smith, New York; New York Homeopathic Medical College and Flower Hospital, New York, 1920; aged 46; died, May 13, of carcinoma of the liver.

Coral Adelbert Lilly @ Ann Arbor, Mich.; Rush Medical College, Chicago, 1901; aged 62; died, May 3, in the University Hospital of atherosclerosis with aneurysm.

Joseph M. Campbell, East Moline, Ill.; Missouri Medical College, St. Louis, 1880; formerly St. Clair County coroner and sheriff; aged 86; died, May 15, of uremia.

Robert Nichols, Houston, Texas; Eclectic Medical University, Kansas City, Mo., 1912; aged 59; died, May 30, in the Memorial Hospital of hyperthyroidism.

George Schmucker Frank @ Millheim, Pa.; Jefferson Medical College of Philadelphia, 1883; bank president; at one time county coroner; aged 80; died, April 13.

Lemuel K. Chandler, Tucson, Ariz.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1935; aged 31; died, May 20, of rheumatoid arthritis.

Samuel J. Drummond @ Casnovia, Mich.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1897; aged 73; died, April 28, of pneumonia.

Frederick Richmond Adamson, Abilene, Texas; University of Nashville (Tenn.) Medical Department, 1900; aged 66; died, May 28, of coronary occlusion.

Charles Clifton Scott, Princeton, Ill.; Rush Medical College, Chicago, 1891; member of the Illinois State Medical Society; aged 73; died, April 3.

William Canova Peterson Jr., Wilmington, N. C.; University of Virginia Department of Medicine, Charlottesville, 1917; aged 49; died, April 10.

Pietro C. Blasi, Mount Vernon, N. Y.; Regia Università degli Studi di Roma, Facoltà di Medicina e Chirurgia, Italy, 1897; aged 66; died, April 3.

Meyer Nuta, Chicago; Universitatea din Bucuresti Facultatea de Medicina, Rumania, 1901; aged 66; died, May 20, of carcinoma of the pancreas.

Israel Fred Stowe, Basco, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1910; aged 65; died, May 5, of cerebral hemorrhage.

John H. Driver, Brownsville, Texas; Arkansas Industrial University Medical Department, Little Rock, 1884; aged 83; died, April 1.

Alonzo Bowen Hyndman, Carp, Ont., Canada; McGill University Faculty of Medicine, Montreal, Que., 1915; aged 49; died, April 9.

George Edward Chappell @ Sacramento, Calif.; College of Physicians and Surgeons of San Francisco, 1905; aged 62; died, April 3.

Jacob Hall, Kansas City, Mo.; Eclectic Medical University, Kansas City, 1902; aged 81; died, May 7, of cerebral hemorrhage.

Laura Ewing Reading, Tampa, Fla.; Woman's Medical College of Baltimore, 1885; aged 89; died, May 12, of chronic myocarditis.

John Fletcher Douthitt, Dover, Ohio; Starling Medical College, Columbus, 1898; aged 65; died, May 6, of coronary thrombosis.

Werner Hiltbold @ Easthampton, Mass.; University of Vermont College of Medicine, Burlington, 1912; aged 50; died, April 5.

Joseph Walter Rogers, Macon, Ga.; Louisville (Ky.) Medical College, 1889; aged 82; died, May 1, of chronic cystitis.

Charles Henry Moncure, Orange, Va.; Medical College of Virginia, Richmond, 1880; aged 81; died, May 11, of uremia.

Frederick George Metzger @ Carthage, N. Y.; University of Buffalo School of Medicine, 1907; aged 57; died in April.

Jacob Coy Bucher, Alpena, Mich.; Medical College of Ohio, Cincinnati, 1878; aged 86; died, April 23, of senility.

Albert Hathaway @ Edon, Ohio; Rush Medical College, Chicago, 1881; aged 90; died, May 9, of heart disease.

John McLean, Hartford, Mich.; Chicago Medical College, 1873; formerly health officer; aged 100; died, April 26.

William Turner Morris @ Wheeling, W. Va.; Pulte Medical College, Cincinnati, 1902; aged 60; died, April 30.

Samuel Proctor Kerns @ Philadelphia; Jefferson Medical College of Philadelphia, 1892; aged 77; died, April 7.

Hugh Horace Ross, Seaforth, Ont., Canada; University of Toronto Faculty of Medicine, 1896; died, April 8.

J. D. L. Ball, Milton, W. Va. (licensed in West Virginia in 1888); aged 89; died, May 2, of senility.

Correspondence

FRACTURE OF THE POSTERIOR ARCH OF THE ATLAS

To the Editor:—The authors of the clinical note "Fracture of the Posterior Arch of the Atlas" (Sinberg, S. E., and Burman, M. S.: *THE JOURNAL*, May 18, p. 1996) present two cases with instructive roentgenograms and follow-up histories.

They describe the mechanism of the injury as pressure of the occiput on a "rigid cervical spine with the muscles of the neck relaxed." As a rule muscular fixation seems to be essential in producing a fracture of the atlas in this squeezing action. The authors are kind enough to refer to two short articles of mine on the subject, while the more detailed paper "Fractures of the Atlas Resulting from Automobile Accidents: A Survey of the Literature and Report of Six Cases" (*Am. J. Roentgenol.* 40:867 [Dec.] 1938) apparently has escaped their attention. Sinberg and Burman conclude that fracture of the posterior arch does not seem to be an independent fracture but is associated with fractures of the cervical spine at other points. One can agree with this statement only for the majority of atlas fractures. Table IVb of my more detailed paper lists fifty-nine cases of concurrent injuries of the remaining spine, while table IVa lists forty cases of isolated fractures of the atlas, many of them confined to the posterior arch.

H. F. PLAUT, M.D., Mansfield, Ohio.

TESTS FOR CONCENTRATION OF ALCOHOL IN BLOOD

To the Editor:—The communication to this department by Dr. Leake and his associates (*THE JOURNAL*, March 23, p. 1098) wherein purported evidence was given to support a claim of unreliability of the Heise method for determining the concentration of alcohol in the blood has been ably answered by Dr. Heise (April 6, p. 1391) and by Dr. Harger (April 27, p. 1687). However, owing to the damage to the validity of such tests as criteria for stages of intoxication which this communication from Dr. Leake has undoubtedly caused and at the insistence of Dr. Heise, my associates and I decided to offer the following as additional refutation of Dr. Leake's claims.

Fifty specimens of human blood were taken by us over a period of two weeks from patients sent to the laboratory for various blood tests from the eight clinics which this department conducts. These patients were composed of men, women and children. Some were patients under treatment in the venereal clinic, some were diabetic patients and some were patients with nephritis.

All specimens were obtained in a deliberately careless manner. Alcohol was used to sterilize the skin thoroughly and no attempt was made to wipe the arm dry.

All specimens were distilled at the maximum rate possible—so fast that all distillates showed some degree of yellow color due to traces of picric acid carried over by the excessive rate of distillation.

All distillates were run undiluted. There was no detectable reduction of the dichromate solution in any of the fifty specimens.

Finally, three pooled 50 cc. specimens were made up to a concentration of 0.4 per cent by volume with lactic acid (twice the highest reduction claimed by Dr. Leake) and each was distilled. No detectable reduction in the undiluted distillate was observed in any of the three prepared specimens.

I have had experience with some 300 consecutive tests for drunken driving over the past three years. This, coupled with a knowledge of the literature on the subject, made Dr. Leake's contentions too fantastic to be considered valid. However, no

definite effort has ever been made, to the best of my knowledge, to support the reasoning from physiologic and chemical principles involved, which make such claims as those of Dr. Leake untenable, by positive proof in the form of any significant number of tests on normal bloods. Hence the foregoing experiments.

Such communications result in charges that there is no agreement among experts as to the specificity of chemical tests for intoxication. One such published statement from a well intentioned but misinformed source can undo the results of years of painstaking work on the part of recognized authorities in this field.

DONALD F. BAVIS, B.Sc., Lincoln, Neb.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SENSITIVITY TO RAGWEEDS AND COCKLEBUR

To the Editor:—A patient with hay fever was found to give a strongly positive reaction to the pollens of ragweed and cocklebur, especially the latter. Should I desensitize him against both of these pollens or do you think that desensitization with ragweed alone (giant and dwarf) will build up antibodies against the proteins of cocklebur as well, as the two belong to the same botanic group (Ambrosiaceae)?

M.D., Connecticut.

ANSWER.—Although the pollen of cocklebur is not profuse in the air, it is present in small amounts and therefore it should be incorporated in a mixture with ragweed. Because of the overabundance of ragweed, one would suggest that the mixture contain 45 per cent giant ragweed, 45 per cent small ragweed and 10 per cent cocklebur.

INTRAVENOUS ANESTHESIA

To the Editor:—Please send information regarding intravenous amylal as an anesthetic, indications and contraindications, dosage, dangers contingent on its use and antidotes. If there has been any intravenous anesthesia developed since that is superior, I would appreciate information on it. Is avertin with amylene hydrate as rectal anesthesia in good repute and general usage, and are methods of administration and dosage determination about the same as described in M. D. Nosworthy's "Anesthesia" published in 1935?

George Jennings, M.D., Buhl, Idaho.

ANSWER.—Sodium amylal for intravenous administration as a general anesthetic is seldom used in surgery. It can be used safely only by those who have had much experience and are familiar with the literature concerning such use. The Council on Pharmacy and Chemistry of the American Medical Association does not recommend the use of nonvolatile barbiturate preparations in major surgical procedures. Sodium amylal is occasionally given intravenously to control the convulsions arising in association with eclampsia and tetany, in cyanotic individuals or those moribund from trauma, to control the pain of inoperable cancer, and to facilitate cystoscopic examinations and the incision of abscesses, or as a basal anesthetic.

The dose for an adult is usually 1 grain (0.065 Gm.) given in a series of graded doses. If the needle is not removed from the vein, more may be injected intravenously as necessary. Larger doses may be needed for some patients but smaller doses may suffice for others. After the first dose has been given intravenously, succeeding doses are often given to advantage through a nasal or stomach tube, the dose usually being 1 grain (0.065 Gm.) at a time, given intermittently, according to the patient's reaction.

The commonest danger is the obstruction of the respiratory passage by the tongue falling back and covering the glottis. The patient therefore should ordinarily be turned on his side or the head lowered with the jaw supported if the air passage is not clear. Like other barbiturates, sodium amylal is a respiratory depressant and any antidotes given should be those which stimulate respiration. The fall in blood pressure must be combated with circulatory stimulants and intravenous infusion of fluids. Included in the antidotes are metrazol, picrotoxin, nikethamide, ephedrine, solution of epinephrine hydrochloride, and solution of posterior pituitary U. S. P. Metrazol and picrotoxin are agents which must be used with caution. Postopera-

tive manias or excitement may require close supervision for hours. Since there is a tendency for pulmonary edema to develop after large doses of sodium amylal, administration of oxygen and carbon dioxide may be used. The patient should be turned in bed from time to time so that pulmonary edema will not develop in the dependent portion of the lung.

One of the newer and better intravenous anesthetics is pentothal sodium. It is not recommended in major operative procedures requiring long anesthesia or for office procedures.

Avertin with amylene hydrate as a rectal anesthetic is not used as much as formerly. However, it is frequently used for a basal anesthetic, supplemented by a local or general anesthetic. The doses described in M. D. Nosworthy's "Anesthesia," published in 1935, are satisfactory.

URTICARIA AND COLITIS

To the Editor:—In April 1931 a man then 32 years old had a septic sore throat which was treated by his physician with intravenous injections of acriflavine hydrochloride 20 cc. per session. On one of these occasions the fluid was injected paravenously, intra-arterially and into the left elbow joint, with resulting severe reactions leaving the patient finally with a paralysis of the median and ulnar nerves. As the result of a law suit he was enabled to receive the best of care available and traveled all over Europe in order to get the use of his left hand back again. During all this time he refused to be given morphine for the excruciating pain and was given a combination of codeine acetylsalicylic acid and acetophenetidin. After he had spent almost two years in different institutions abroad, his hand finally had improved so much that he is able to hold a newspaper or a comb. He still cannot bind his own ties. About 1934 he noticed the appearance of hives all over his body, with temperatures up to 104 F. and glottis edema, which at one time almost necessitated a tracheotomy. Scratch and intradermal tests, however, never gave positive reactions to anything except peptones and polypeptides. After proteins had been eliminated from his diet, the hives and itching disappeared for about two weeks and returned. He has since been treated with dry pepsine prepared from fibrin, histaminase, calcium gluconate (which aggravated his condition considerably while he took it), pancreas therapy, and finally old tuberculin, starting with 0.1 cc. of a 1:100,000 solution and increasing to 0.98 cc. of a 1:100 solution. While these daily injections were being given the urticaria became less and less frequent, until after eighty injections he was able to eat everything, including meats, milk and eggs, without getting a reaction. This lasted for about six months after the last injection of old tuberculin. Then he suddenly had colitis, bloody slimy diarrhea and return of his urticaria. Old tuberculin was resumed but with less success, for he had changed his town and the doctor was afraid to go ahead with a daily dose. So it was given with a four day interval for about three months. All this time the patient was watching his diet and carefully avoided milk, eggs and meat, not to mention alcohol, but he had occasional urticaria just the same. When he came to New York he was free from symptoms. He has been here for two and one-half months. During this time he has been able to go for two weeks or ten days without having to watch his diet and then suddenly finds urticaria on his feet, arms or body. This time, however, his face and lips have not been attacked as yet. One week ago he ate pancakes and within twenty-four hours was seized with another attack of bloody diarrhea and large hives all over his body, about 0.25 cm. high, with dark red or bluish edges. Ephedrine has not relieved him at all. Now he has no diarrhea but complains of dull pain along the colon and of course intense itching of the urticaria. Examination revealed almost complete lack of the pancreatic juices. The feces show a large amount of undigested proteins. I would greatly appreciate it if you would advise me whether there is any known relation between colitis and urticaria and which is the primary cause, the colitis producing the allergic reactions or the allergy producing the colitis; whether anything is known about the role of the pancreas in allergy, whether there is any known reason for the relief obtained by old tuberculin, what could be done as far as treatment of this case is concerned and whether there is any chance of this man ever recovering from his condition.

Kurt T. Shery, M.D., Jackson Heights, N. Y.

ANSWER.—There is no clear indication that the injections the patient received in 1931 and the subsequent local complications have any bearing on the present syndrome of urticaria and colitis. Disturbed bowel function, such as abdominal pain, discomfort, gaseous distention, spasmodic diarrhea, spastic constipation and a tender colon are frequently the result of allergic irritation of the gastrointestinal tract and are thus rather frequent accompanying symptoms in urticaria. Blood in the stools is less frequent but does occur. It is likely, therefore, that one is dealing here with an allergy involving both the skin and the bowel. The acute reaction described after eating pancakes should make one particularly suspicious of buckwheat as a possible allergen. However, there is also a possibility that the bowel dysfunction is responsible for the urticaria. This may be due to one of several reasons. An inflamed bowel may result in an increased permeability of its wall with the easier entrance of the food allergen into the circulation. An intestinal infection or an abnormal bacterial content may presumably be responsible for an allergic substance arising directly from the bacteria or from the products of bacterial action on food residues. It should also be kept in mind that the bowel disturbance may be a symptom of parasitic infestation and that the latter may be the cause of a remote urticarial allergy.

The role of the pancreas in the mechanism of allergy is not settled. There is common belief that foods are apt to cause less allergy if they are well digested, and pancreatic enzymes as well as hydrochloric acid, pepsin and bile salts have been suggested as therapeutic measures. A theory has also been presented (Oelgetz, A. W.; Oelgetz, P. A., and Wittekind, Juanita: Studies in Food Allergy: Preliminary Report, *Ann. J. Digest. Dis. & Nutrition* 1:730 [Dec.] 1934) that hypersensitivity to food is caused by an excess of undigested food protein in the blood serum and that this excess is due to a low concentration of pancreatic enzyme in the serum. The latter, in turn, is due to an insufficient pancreatic enzyme mixing with the food in the intestinal tract. The weakness of these "absorption" theories is that it has been shown that proteins in their normal antigenic state are absorbed from the gastrointestinal tract and that in the allergic individual such absorption is not increased. As a matter of fact, for reasons not entirely clear, this absorption tends to be diminished in the allergic person.

The employment of old tuberculin in allergic conditions is based on the theory that the use of a specific allergen to which a person is sensitive creates a certain amount of resistance to other allergens. Since tuberculin allergy is common it is not natural to proceed to that type of allergic therapy when the allergen causing the complaint is not identifiable.

An attempt should be made to study the patient along the lines suggested. The possibility of bacterial infection or parasitic infestation should be considered by direct examination of the gastrointestinal tract and by intracutaneous tests with extracts of common parasites (*Ascaris*, tapeworm, pinworm and the like). Since the food tests have been unsuccessful, the scheme of a food diary record might throw some light on a possible food allergy. A leukocyte count following the ingestion of individual basic foods may enable one to determine which foods one can rely on to form a basic but restricted diet (Vaughan, W. T.: Further Studies on the Leukopenic Index in Food Allergy, *J. Allergy* 6:78 [Nov.] 1934). If food allergy or other specific allergy cannot be ascertained, more or less nonspecific therapy will have to be tried. Histaminase may be given a trial, although the evidence at hand does not indicate much possibility of usefulness of this material. Histamine in small doses, beginning with 0.1 cc. of a 1:5,000 dilution and increasing to about 1.0 cc. by daily subcutaneous injections may produce benefit. Autohemotherapy with from 10 to 20 cc. of blood is sometimes efficacious. As already suggested, pancreatic enzyme and other digestive aids would also be worth trying. With regard to chances of recovery, one can epitomize the status of therapy of urticaria by saying that almost every case is difficult and that no case is hopeless.

TESTING FOR RADIOACTIVITY

To the Editor:—Is there a method available to determine the amount of radioactive substances (thorium B in particular) in the blood and spinal fluid? Roeder has worked with an "electrometer" and has published his experiments in a German journal (*Ztschr. f. d. ges. Neurol. u. Psychiat.* 161:553, 1938). Is there an "electrometer" available in this country?

M.D., Massachusetts.

ANSWER.—For several years the only known method for testing small amounts of radioactivity in the bodies of dial painters during life and after death was by means of electrosopes and gamma electrometers.

Two methods were originally employed to detect and estimate the radium in the body during life. First, by placing the patient before a gamma ray ionization chamber electrometer, measurements were made of the gamma radiations coming from the body, penetrating rays given off by radium C, which is a decay product of the radon retained in the body. The quantitative evaluation of radium C thus made is expressed in terms of the amount of radium required to produce it.

Secondly, radon estimations were made by collecting the expired air in the ionization chamber of an electroscope and determining the amount of radon or thoron (emanation from mesothorium) present. In old cases of radium poisoning approximately 45 per cent of the total amount of radium in the body gives rise to radon which escapes in the expired air; the subsequent decay products of this exhaled radon, including radium C, are, therefore, formed outside the body.

The measurement of this radon can be expressed in the amount of radium required to produce it. This test is also a check on the first method, determining whether radium, mesothorium or both are present, and in estimating the total radioactivity the sum of the two tests gives the total amount of radium present in the living body.

It was found that the methods as described were not sensitive enough for the detection of small amounts of radioactivity in former dial painters who were exposed from fifteen to twenty

years previously and who were still dying from osteogenic sarcoma. Nor were these methods reliable enough to detect radium poisoning in present dial painters, so that they could be removed from their exposure and elimination methods instigated.

Recently devised gamma ray detectors and direct reading counting rate meters, based on the principle of the Geiger counter, permit of more rapid and accurate estimations than electrometers and have replaced earlier methods in the diagnosis and estimation of radium poisoning. Highly sensitive quantum counters detect gamma radiation from 0.2 microgram of radium, whereas by the best electroscopic examinations the detection of less than 5 micrograms of radium in the living body was exceedingly difficult and often impossible.

These newer methods are fifty times more delicate than the older ones. Furthermore, by means of emanation methods even smaller amounts (almost to infinity) can be detected. Such methods are now in use in the detection of artificial radioactive elements (such as radio-iodine prepared by means of the cyclotron and used in experimental medicine as tracers) and in the identification and measurement of radioactive substances in the blood, feces, urine and the like.

Robley D. Evans, Professor of Physics at Massachusetts Institute of Technology, has originated and perfected many of these newer methods. Under a grant-in-aid from the National Cancer Institute, Professor Evans constructed a gamma ray detector, and a station for the detection of radium poisoning has been established in Newark, N. J. It is believed, however, that emanation methods are the most desirable.

MENORRHAGIA AND METRORRHAGIA

To the Editor:—A white woman aged 21, a virgin, has had irregularity in the menstrual periods ever since the onset of the menses, which occurred at 13 years of age. At times a menstrual period may not occur for three or four months, while at other times a period, when it does occur, may last from three to four weeks. The patient states that two and one half years ago one period lasted five weeks, two pads a day being necessary up to the time of the cessation of the flow. She came to see me Jan. 2, 1940, with a similar complaint. Her period began Nov. 21, 1939, and she has had vaginal bleeding since. Physical examination revealed an increased amount of hair on the arms and legs and a mole distribution of the pubic hair. The blood pressure was 120 systolic, 80 diastolic. Nothing was palpated in the pelvis on rectal examination. The hemoglobin was 60 per cent (Sohli). I am interested in a diagnosis in this case. I can think of a few conditions which might be etiologic factors: 1. Hypothyroidism, though the clinical picture does not resemble this condition. The patient is of average height and weight for her age, does not fatigue easily, perspires freely and has a good appetite. Unfortunately the basal metabolic rate has not been determined as yet because I feel that the patient's anemia would distort the result. 2. An adrenal cortical tumor because of the hypertrichosis. However, the patient has no hypertension and I believe that such tumors result in either complete amenorrhea or oligomenorrhea. 3. Increased estrogenic hormone secretion. I have thought that this might be a causal factor because of increased follicles in the ovary. I have not, however, as yet had a quantitative urine estrogenic hormone determination. 4. Insufficient gonadotropic secretion of the pituitary gland, resulting in inadequate control of the menses by inadequate stimulation of the ovaries. I would appreciate any information that would help toward arriving at an accurate diagnosis and any aids in therapy which would result in regularity of the menses. The flow finally ceased two days ago after treatment with iron, calcium, ergot and bed rest. The patient is a school teacher and such bouts of menstrual bleeding are incapacitating, requiring her to lose time from her work. Might a course of anterior pituitary-like hormone be tried fourteen days or so before the supposed onset of the menses? Might small doses of desiccated thyroid be of help, though the symptom picture does not resemble hypothyroidism? M.D., New York.

ANSWER:—The menstrual irregularity of this patient does not appear to be the result of a general endocrine disturbance but seems to arise in an ovarian dysfunction alone. Endometrial biopsies are desirable in order to try to make a more definite diagnosis. Excessive bleeding due to hypothyroidism would respond satisfactorily to thyroid therapy. One or more basal metabolic tests should be made on the patient in order to prove or disprove the diagnosis of hypothyroidism. It is questionable whether thyroid therapy is of value in cases in which there is not a low basal rate or other signs of hypothyroidism. The anemia demonstrated by this patient will not interfere much with the basal metabolic studies.

Chorionic gonadotropic (formerly called "anterior pituitary-like") substance is said to control bleeding of the menorrhagia type. There is some question as to whether women in the child-bearing age respond as favorably as those near the menopause. The doses usually used are from 300 to 400 rat units hypodermically two or three times a week for one or two months. Administration of testosterone propionate has been used successfully to control menorrhagia and metrorrhagia. The doses usually administered are 10 to 25 mg. hypodermically two or three times weekly for about a month. This therapy is still experimental.

An attempt should certainly be made to overcome the anemia, stimulate red blood cell formation and build up the patient as regards her nutrition. If the patient does not bleed profusely or too long a time, there is little need for concern as regards the irregularity of the menses. After marriage, however, if the patient is sterile and desires children, attempts can be made to regulate the cycle.

ARTIFICIAL MENOPAUSE AND ESTROGENIC THERAPY

To the Editor:—A woman aged 29 has had six children and one year ago a hysterectomy was performed. Since the operation she has complained of severe headaches, dizziness and extreme weakness. I do not know why the hysterectomy was performed but apparently it was done for subinvolution. Her general physical examination is entirely negative including an ophthalmoscopic examination and the proper fitting of glasses. She was started on theelin about one year ago when I first saw her. At first she had 2,000 unit doses three times a week with no improvement. Later the dose was increased to 10,000 units. For a while she felt better on this regimen but lately she has become much worse. 1. What are the symptoms of overdosage with estrogenic substance? 2. If the ovaries are left in at the time of hysterectomy will they function normally throughout the sexual life of the patient or do they soon undergo change?

M.D., Michigan.

ANSWER:—Presumably the reason the patient is not being relieved of her headaches, dizziness and extreme weakness is that she is not receiving large enough doses of estrogen. She may be given 50,000 international units of estrogen hypodermically once a week for three weeks and then 10,000 international units once a week for three or four more weeks. Following this or concurrently with it, the patient may take 2,000 or 4,000 international units of estrogen by mouth. She will have to increase this dose if the symptoms are not relieved and contrariwise she should take medication only once every second day if she is relieved. After a few weeks the patient can usually work out a satisfactory dosage for herself. Estrogenic therapy might have to be continued for a long time. It is assumed, of course, that a thorough examination has been made to make certain that there is no other cause for the distressing symptoms than the hysterectomy, and the matter of a possible history of cancer in the family should be considered.

1. Women can tolerate large doses of natural estrogen without disturbing constitutional signs or symptoms. Although ovarian disturbances may occur, it is conceivable however, that after prolonged administration women may develop headaches from an enlarged pituitary gland. Likewise there is the possibility that mammary or uterine carcinoma may be favored.

2. There is no unity of opinion on this subject. It is generally believed that the ovaries do continue to function after the uterus is removed. However, many gynecologists hold that this is not so; hence they remove both ovaries whenever they perform a hysterectomy. There seems to be no doubt that far fewer women have distressing menopausal symptoms following hysterectomy alone than after hysterectomy and bilateral oophorectomy. Furthermore, many women who have a simple hysterectomy do not have a change of life until a number of years after the hysterectomy.

SALT AND CARBOHYDRATES IN HEADACHE

To the Editor:—Has there been any research on the use of sodium chloride in the treatment of migraine or "sick headache"? I am not subject to frequent headaches but when I do have one it is severe. Recently when one started I felt too nauseated to take any anodyne but had a craving for salty potato chips. I thought it could do no permanent damage to try some. The relief was immediate and dramatic. The questions in my mind are these: Could the anion of the sodium chloride be responsible for the relaxation of the smooth muscle? (I understand there is a pylorospasm.) Could this medication be of therapeutic value? Was it a coincidence? Having been called to treat so many cases of "nervous headaches," one is apt to grasp at a straw. M.D., California.

ANSWER:—There have been as many different treatments for migraine as there have been theories regarding its etiology. It seems probable that the syndrome has different causes in different individuals, and that the success of a particular treatment varies accordingly.

Villey and Buvat (*Paris méd.* 1:189 [Feb. 27] 1937) reported relief of migraine in three cases following the intravenous injection of 20 cc. of a 10 per cent sodium chloride solution. They attributed their results to the alleviation of cerebral edema. On the other hand, Gerson (*W'ien. Klin. W'chschr.* 45:744 [June 10] 1932) previously claimed favorable results in decreasing the incidence and severity of attacks from the use of his diets which were low in salt content.

If there was indeed a cause and effect relationship between eating the potato chips and the relief of headache in this case, the result might also have been due to the carbohydrate content of the potatoes. Here again, the literature is contradictory.

Gray and Burtress (*Endocrinology* 19:549 [Sept.-Oct.] 1935) reported that in certain cases of migraine the attacks coincided with periods of relative hypoglycemia and were successfully treated by frequent carbohydrate feedings. But there are, on the contrary, a number of reports (e. g. Wagner-Jauregg: *Wien. med. Wchnschr.* 85:1, 1935; Porges: *Med. Klin.* 33:664 [May 14] 1937) purporting to show that a low carbohydrate diet exerts a beneficial influence over extended periods of observation.

SLIGHT GENERALIZED EDEMA

To the Editor:—A married woman aged 34 has acquired a mild but persistent generalized edema. It was noticed in the feet and ankles some two months before it was present in the face, eyelids, arms and breasts, which began about Nov. 1, 1933. She describes the skin as feeling "thicker" all over and feels that the appearance of her face has changed. For the past few weeks, however, the edema has become less in the face again and more in the legs. She feels that the left leg swells slightly more than the right and has noticed that the veins behind the left knee have enlarged during this time (confirmed by examination). Except for the unpleasant swelling of her skin, the patient admits only that she is not quite so strong as previously and that she feels slightly feverish at times. She is able to continue her regular duties as a housewife with two children to take care of. She has never been pregnant, the children being her husband's by a former marriage. Her past history is uneventful except for an attack of sinusitis (of the left antrum) fifteen years ago with a recurrence though of a mild nature, which subsided rapidly without treatment about the middle of October 1933. The patient is a woman of normal appearance weighing 125 pounds (57 Kg.). Examination, which included transillumination of the sinuses, was negative except for a slight systolic blowing murmur, a somewhat eroded cervix, a moderately retroflexed uterus and slight but definite pitting edema of the ankles and legs. The swelling of the skin of the face, arms and breasts was not so definite but the feeling of abnormal thickness to the skin was insisted on by the patient. (She is a former registered nurse and there is no trace of neuroticism.) The temperature 99.4 F (by mouth), pulse 72, blood pressure 114/66, basal metabolic rate plus two, urine normal as to albumin, sugar, concentration and microscopic examination on several occasions, blood protein content: albumin 4.5, globulin 2.25, total proteins, 7.25, sedimentation time 11.5 mm. in one hour (Cutter tube), hemoglobin 75 per cent (Sahli); white count 4,200, with an essentially normal differential count. I have tried the following treatments to no avail whatever: diluted hydrochloric acid, salt poor diet, high vitamin diet and desiccated thyroid tablets, 1½ grain (0.1 Gm.) daily for ten days. I do not see how a mild infection such as suggested by the slight increase in sedimentation time and the slight fever could cause such edema even if it could be located. Can you throw any light on this perplexing case for me? I should greatly appreciate any leads you might suggest and would hasten to follow them up.

M.D., New York.

ANSWER:—The usual systemic causes of edema seem to be rather clearly ruled out in this case. A cardiac, renal or metabolic edema would not fit the physical and laboratory observations. The physical examination reveals a slight pitting edema of the lower extremities. Such a condition could be the result of local causes, either obstruction to the return circulation or venous incompetence. The combination of fever, increased sedimentation rate and leg edema suggests a pelvic infection. It is possible, although highly improbable, that an abdominal Hodgkin's disease might present this picture. Such a diagnosis would assume that some enlarged glands within the abdomen cause pressure on the return circulation.

None of these, however, would cause generalized edema in the case described. It would seem best to reserve judgment about the generalized edema until it had been personally observed.

ESTROGENIC HORMONES AND URTICARIA

To the Editor:—I am treating a white woman, aged 51, for menopausal distress with estrogenic hormones and am having some difficulty with urticarial eruptions following treatments. The patient states that she used to have eczema some years ago. I have given her estrogens biweekly at first, and lately only once a week. I have tried different preparations, all with the same result. She is greatly improved as regards the menopausal symptoms, but I am forced to discontinue therapy because of the undesirable side action. Can you tell me if this has been observed by other physicians and if there is some way to treat this patient and avoid the ill effects? Would oral preparations be apt to produce the same ill effects?

M.D., Minnesota.

ANSWER:—It is quite possible that the patient is not sensitive to the estrogenic hormone but is sensitive to the vehicle employed as a solvent, in this case the particular oil plus the preservative used in the solution, if any.

The question is asked "Would oral preparations be apt to produce the same ill effects." Oral preparations, if they do not contain the substance to which the patient is sensitive, should not cause any difficulty, provided the patient is not sensitive to estrogenic substance. That the patient is sensitive to an estrogen is possible but improbable and can easily be determined by the methods described.

SENSITIVITY TO WOOL FAT

To the Editor:—I have received an inquiry as to the frequency with which lanolin produces skin rashes. My own impression is that lanolin is about as bland a substance as can be applied to the skin. I have never heard of any one who was allergic to it. Are there any available statistics on the subject?

Norman P. Rindge, M.D., Clinton, Conn.

ANSWER:—There are few reports in the literature of sensitization to wool fat. The only ones found in the American literature are those by M. A. Ramirez and J. J. Eller (*The Patch Test in Contact Dermatitis [Dermatitis Venenata]*, *J. Allergy* 1:48 [Jan.] 1930) and by M. B. Sulzberger and J. L. Morse (*Hypersensitivity to Wool Fat*, *THE JOURNAL*, June 20, 1931, p. 2099). Each paper reports two cases, all of them with positive patch tests to wool fat. One of the patients of Sulzberger and Morse was a wool salesman in whom the patch test to wool was weakly positive. The other patient, a dress designer, had a negative patch test to wool. Both gave no reaction to scratch tests. This paucity of reports of sensitivity to wool fat does not indicate that it is an uncommon phenomenon but that it is not considered remarkable enough to warrant reporting. Dermatologists see it not infrequently. Sézary remarks that it is seen often than sensitization to petrolatum (*Intolerance cutanée à la lanoline*, *Presse méd.* 44:1880 [Nov. 18] 1936).

PAPULAR LESION IN CHICKEN FEATHER PICKERS

To the Editor:—I am plant physician to a chicken dressing factory. During the last month I have seen about fifteen girls with large numbers of warts mostly on the palmar surface of their hands. All of these girls have been feather pickers and pin feather pickers. The lesion starts as a deep pin point papule; this breaks down, discharging serous material, and then over a period of a few weeks a tender wart forms. Although irritation seems to play a big part, a few of the girls have warts on the dorsal surface of their fingers and one of them on her knee, on which there seems to be no source of irritation. The chickens have already been dipped in boiling water and molten wax for ten seconds, which would seem to suffice for superficial sterilization. Besides avoiding irritation, what would you advise for treatment and prevention? The water used at the plant has significant amounts of iron and sulfur in it. Would this influence the picture?

S. M. Berger, M.D., Selbyville, Del.

ANSWER:—The warts noted on these girls are no doubt the result of a foreign body reaction resulting from the embedding of particles of feathers, e. g. quill, shaft, pith, barbs or vane, which penetrate into the epithelial layers and produce a wart at the site. Lesions of similar type have been described in asbestos workers by A. P. Dewirtz (*Arch. f. Dermat. u. Syph.* 161:1, 1930). He describes the occurrence on the inner surface of the hands, more often the right, of from three to five and occasionally more efflorescences which morphologically resemble a non-inflammatory papule. Some are round, others angular with a rough surface, and they are usually situated in the epidermis at a point that corresponds to the penetration point of an asbestos needle in the skin. This disease has a definite localization on the palm and closely simulates the ordinary warts seen in workers in asbestos pits and is rare in other sections. The disease is produced through the penetration of the asbestos crystals into the epithelial layers. At the site of the layer there appears an extensive proliferation of cellular elements with the development of giant cells and marked cornification, and as a reaction there develop in the underlying tissue the signs of a chronic inflammatory process.

For prevention, the best approach would be to have the workers wear sturdy gloves made of rubber or one of the newer elastic fabrics. Soluble iron or sulfur in the water would not act as foreign bodies or be likely to influence the picture.

VITAMIN E

To the Editor:—Is vitamin E in large or small doses safe to administer to patients for a long period of time? I was informed that in experiments on rodents large doses predisposed to cancer. It has been suggested in lateral spinal sclerosis, also in the third stage of tabes. In both of these I question its value.

A. G. Sogge, M.D., Buffalo.

ANSWER:—Four or five laboratories have endeavored without success to confirm the claim originally made by Rowntree that the feeding of crude wheat germ oil produced cancer in rats. Crude wheat germ oil, a purified product, and concentrates of vitamin E were alike ineffective either in producing cancerous lesions or in modifying their progress. Transplants of mammary carcinoma have been maintained for two and a half years in vitamin E-deficient animals without change in the cytologic character of the growth. Vitamin E thus has no effect on cancer so far as known.

The value of vitamin E in lateral spinal sclerosis remains uncertain. The dystrophy produced in experimental animals

seems to be primarily muscular in origin, and the alterations which have been described in the central nervous system have not been duplicated or confirmed. Accurately controlled clinical experience is greatly needed.

ALCOHOLIC LIQUORS WITH SULFANILAMIDE

To the Editor:—It has long been a question as to whether alcohol in the form of whisky and wines should be taken at the same time at which sulfanilamide products are being administered. Any information that you can give concerning this subject will be appreciated.

Herman C. Quantz, M.D., Bunkie, La.

ANSWER.—Ordinarily, alcohol in the form of whisky and wines should not be administered to patients who are receiving sulfanilamide or its derivatives. It has been observed that two cocktails consumed at a time when the blood concentration of sulfanilamide was 5 mg. per hundred cubic centimeters notably increased the dizziness resulting from the sulfanilamide. In general, alcohol increases symptoms of dizziness, nausea and vomiting, and the inability to coordinate that are frequently seen in the course of sulfanilamide therapy. However, in a seriously ill chronic alcoholic addict whisky would not necessarily be contraindicated because its withdrawal might result in the appearance of delirium tremens or some other form of alcoholic psychosis.

TINTED LENSES FOR MOTION PICTURE OPERATOR

To the Editor:—One of my patients who is a movie operator and is constantly looking at the pictures tells me that a tinted lens such as Crookes A or B saves him considerable eyestrain. He thinks the light is similar to sharp sunlight on the eyes, the tinted lens preventing the rays from striking the eye. Is this true? I have not been able to find any information on this point in any textbook.

David Gloss, M.D., Louisville, Ky.

ANSWER.—The amount of light reflected from the screen in a motion picture house is so infinitesimal as to be negligible in the production of symptoms. However, the operator may be exposed to light from the high intensity source of illumination that is used in projecting lenses. If that is the case a tinted lens will undoubtedly give him the comfort he describes.

DIABETES AND KNOT GRASS

To the Editor:—A patient claims that the use of a certain grass has been effective in controlling his diabetic condition. He claims that it is an old European treatment. He has had this grass examined by a botanist, who identified it as knot grass, *Polygonum aviculare*, a member of the buckwheat family. Is there any scientific or clinical evidence to corroborate his claim?

M.D., New Jersey.

ANSWER.—From time to time one hears or reads reports of success in treating diabetes with herbs, plants or vegetables or extracts of these. Those which have been subjected to well controlled laboratory and clinical trial have not been found helpful. Although work regarding the effect of *Polygonum aviculare* has not been found, it seems safe to assume that this grass would likewise be valueless. It is true that the use of green leafy plants which make acceptable articles in the diet may exert a beneficial effect on patients with mild diabetes because they provide a bulky diet low in calories, but no specific value can be claimed.

NASAL PLASTIC OPERATION AND LIBIDO

To the Editor:—Several of my gynecologic patients who have undergone nasal plastic operations have stated that there has been a definite change in their libido since the operation: a few diminished, more increased. In view of the ancient belief of so-called genital spots on the tuberculum septi and inferior turbinates, might one assume that the operation produced a new nasogenital-sexual relationship? Are there any published reports by plastic or oral surgeons of a large number of cases showing changes in the libido following nasal operations? I do not, of course, refer to the increased attractiveness to the opposite sex engendered by the operation but to actual personal libidinous alterations.

Melvyn Berlind, M.D., Brooklyn.

ANSWER.—There is no anatomic reason for either an increase or a decrease in libido following nasal plastic operations, chiefly because plastic operations on the nose do not involve the tuberculum septi and inferior turbinates. There is, of course, a definite change in personality in most single girls and married women whose noses are beautified by nasal operations. Most such young women feel that they are much more attractive after they have the operation. As far as is known there has not been any published report on the relationship of nasal plastic operations to libido.

POSTPARTUM PSYCHOSES

To the Editor:—Three years ago I delivered a patient who developed a puerperal psychosis about ten days post partum. She had a rather prolonged labor because of an occiput posterior presentation. The delivery was normal. A week post partum she began to talk a lot and write lengthy letters. When she went home, fourteen days post partum, she became nervous and noisy and it became necessary to institutionalize her for a short while. She recovered completely. She remained stout and nervous. Recently she became pregnant again. What can be done to prevent the recurrence of the puerperal psychosis?

M.D., Missouri.

ANSWER.—Postpartum and postoperative psychoses constitute a heterogeneous group consisting of delirious reactions. The patient's entire medical and psychologic situation must be investigated, especially for factors of fear. Postpartum infection or absorption of toxic material are additional etiologic factors. Should this patient have a severe recurrence of puerperal psychosis the question of preventing subsequent pregnancies by contraceptive methods will have to be considered. General physical and mental hygienic measures are the only known prophylaxis, aside from preventing conception in persons subject to recurring postpartum psychosis.

ANKLE CLONUS AND BABINSKI SIGN

To the Editor:—What is the physiologic reflex mechanism involved in (1) a sustained ankle clonus and (2) an unsustained ankle clonus? A patient had tuberculous spondylitis (Pott's disease) with fairly severe kyphos in the low dorsal area and developed a spastic diplegia of both lower extremities. On bed rest and following spine fusion she has regained full use of both lower extremities for more than one year now. For the past few weeks she has been ambulatory and has no complaints. However, on physical examination she has slightly hyperactive deep reflexes in both lower extremities with unsustained but definite ankle clonus on the left. Exploratory operation revealed the spine fusion to be solid its entire length and x-ray examination shows the fusion to be long enough to splint the diseased spine. The Babinski sign is absent bilaterally. In view of these observations does the persistent ankle clonus have any prognostic significance? If the Babinski sign was positive bilaterally but ankle clonus absent in a similar case in which recovery from a diplegia due to Pott's disease was occurring (I have such a case) would there be any difference in the prognosis? In a case of upper motor neuron paralysis does ankle clonus have any significance more than the hyperactive deep reflexes convey? If so, what?

Keith E. Holmes, M.D., Staten Island, N. Y.

ANSWER.—An ankle clonus means a defect in the motor pathways. This is true with both the sustained and unsustained varieties. It has practically the same significance as deep reflexes and a positive Babinski sign, though they are not necessarily concomitant. The Babinski sign indicates a more profound disturbance. The ankle clonus means slightly more than hyperactive reflexes but is on the same order.

TREATMENT OF CONGENITAL SYPHILIS IN PREGNANCY

To the Editor:—How much treatment should a congenital syphilitic patient have in a second and succeeding pregnancies and when should it be started? The positive Wassermann reaction was discovered accidentally. The patient has never had symptoms of the disease. She has received twenty injections of neocarsphenamine and sixty injections of a bismuth compound. The first baby is normal. The mother's Wassermann reaction is always positive.

M.D., Oregon.

ANSWER.—If it is established that the mother has congenital syphilis, it would be one of the really rare occurrences in the biologic course of the disease for her to be able to transmit her infection to a child even though she had never been treated for it. The treatment described is probably adequate for all eventualities, including protection of the mother against any possible recurring active manifestations of her congenital syphilis. Again, provided it is established that the mother is congenitally syphilitic, no further treatment during subsequent pregnancies is advised.

DYEING WHITE HAIR

To the Editor:—This inquiry is not strictly medical but no information can be obtained from beauty parlors or barber shops. I have a client who is only middle aged but has white hair. His face is unlined and his manner vigorous, but since he lost his job two years ago he has had difficulty in getting a job because of his white hair. He is set down as an "old man." Anything he would use to darken his hair would obviously have to be kept up indefinitely. Any suggestions would be appreciated.

Paul R. Howard, M.D., El Dorado, Ark.

ANSWER.—The necessity of dyeing hair in order to get a job is a reflection on the intelligence of employers; but if the man is convinced that dyeing his hair will help him he should have patch tests done before the dye is applied with each dye used. This test should be repeated before each retouching to guard against the possibility of sensitization to the dye acquired during the interval. In this way he will be fairly well, though not absolutely, protected against a dermatitis. According to the

new Federal Food, Drug and Cosmetic Act, dyes of this sort should be labeled "Caution. This product contains ingredients which may cause skin eruptions on certain individuals and a preliminary test . . . (sec. 601a).

SULFAPYRIDINE FOR BACILLARY INFECTIONS

To the Editor:—Will you kindly send me any information that you might have regarding the use of any specific derivatives of sulfanilamide in therapy of any infectious diseases caused by bacilli? M.D., Connecticut.

ANSWER.—Sulfapyridine and azosulfamide (neoprontosil) are the only two drugs on the American market other than sulfanilamide which have been used in the therapy of diseases caused by bacilli. There is but little evidence available regarding the efficacy of azosulfamide in bacillary infections. Sulfapyridine has been used in the treatment of Friedländer's bacillary infections, brucellosis, typhoid, Endamoeba coli infections, especially those of tissues and in the urinary tract, and in Proteus, Bacillus pyocyaneus and other bacillary infections of the urinary tract. The value of sulfapyridine in the treatment of bacillary infections has not been established and at the present time the use of this drug in such infections must be considered as still in the experimental stage.

PRESCRIPTION FOR GLASSES

To the Editor:—Refraction of the right eye when not fatigued gave nearly perfect vision with $-0.50 \times 180^\circ$. After homatrapine with paredrine it gave nearly perfect vision with $+0.50 \times 90^\circ$. The lens prescribed was $-0.25 \times 180^\circ$, $+0.25 \times 90^\circ$. It gave 20/15 vision and no apparent strain. Please criticize the prescription. Is it the exact optical equivalent of -0.25 sphere, $+0.50 \times 90^\circ$? Is either preferable? M.D., Ohio.

ANSWER.—The prescription given is the equivalent of -0.25 sphere: $+0.50c90$, which is what one would ordinarily prescribe from the retinoscopic observations as given. In writing prescriptions, the effect of the crossed cylinder is usually written in the prescriptions as a combination of sphere with the total cylinder, as -0.25 sphere: $+0.50c90$.

NIGHTMARES AND SLEEPWALKING

To the Editor:—The mother of a 12 year old boy who "has nightmares and walks in his sleep" inquires whether there is any help for this condition. Reference books at hand do not give me any help in answering her inquiry. Do you know of any useful advice that I can give her? M.D., California.

ANSWER.—It is important in such cases to be sure first that petit mal is not present and second that the gastrointestinal tract has normal function. It is advised that no food be given for three hours before bedtime and that three-fourths grain (0.05 Gm.) of pentobarbital sodium be given one-half hour before bedtime. Light bedclothes and good ventilation are important during sleep.

AIR IN TISSUES

To the Editor:—In connection with the inquiry regarding absorption of air by tissues (The Journal, February 24, p. 680), I report a personal incident. In a carriage runaway I was thrown out, the carriage was tipped over on top of me and I was dragged some yards with the hub cap of the carriage wheel against the lateral surface of my right leg, just above the knee. This resulted in a deep, semicircular laceration which penetrated the skin and fascial planes down into the deeper muscular tissues. Three hours later, following ordinary treatment which consisted of washing out this wound and others with soap and hot water and applying iodine freely, plus sterile gauze dressings (also antitetanus injections), I noted a distinct area of swelling of the thigh, with pronounced crackling sounds when touched by the fingers and expulsion of air from the lacerated wound. This area extended along the lateral surface of the thigh from the knee joint upward approximately 12 inches and was from 3 to 5 inches wide. Being entirely alone, without professional consultants of experience, I naturally thought of "gas gangrene" and that night when two capable surgeons happened to be passing through I eagerly called them in for advice. Fortunately the extent of the area had not increased (I had marked it on the surface), but they both felt that liberal incisions to release the "gas" were called for. However, it was my leg, and I did not feel that gas could develop so rapidly and so temporized until the next morning. During the night I could feel and hear the escape of air from time to time through the laceration, and by morning the area of crackling had decreased nearly 50 per cent, but it was not until forty-eight hours after the original wound that all the air had passed out. I could feel that the air was not only subcutaneous but in the deeper muscular tissues as well, owing probably to the twisting, circular action of the hub of the wheel, which had loosened the various deeper structures and allowed air to pass in. Without any treatment other than occasional changing of the dressing, the unsutured wound healed by first intention in eight days. There was, of course, no way of measuring the actual amount of air that had penetrated into the tissues, but from the area involved and the amount that actually passed out of the tissues, I would estimate that between 200 and 300 cc. of air had entered.

Hartman A. Lichtwardt, M.D.,
American Hospital, Hamadan, Iran.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, June 29, page 2588.

STATE AND TERRITORIAL BOARDS

ALASKA: Juneau, Sept. 3. Sec., Dr. W. W. Council, Box 561, Juneau.

CALIFORNIA: Oral examination (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, July 15. Written examination, Los Angeles, July 15-18. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

CONNECTICUT: Written, Hartford, July 9-10. Endorsement, Hartford, July 23. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. Homeopathic, Derby, July 9-10. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Examination, Dover, July 9-11. Reciprocity, Dover, July 16. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: Basic Science, Washington, Oct. 21-22. Sec., Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Basic Science, Gainesville, Nov. 1. Applications must be on file not later than Sept. 16. Sec., Dr. John F. Conn, John B. Stetson University, De Land.

IDaho: Boise, Oct. 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Oct. 1-3. Superintendent of Registration, Mr. Lucien A. File, Springfield.

IOWA: Basic Science, Des Moines, July 9. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MASSACHUSETTS: Boston, July 9-11. Sec., Dr. Stephen Rushmore, 413-F State House, Boston.

MONTANA: Reciprocity, Helena, Sept. 30. Written, Helena, Oct. 12. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: Basic Science, Lincoln, Oct. 1-2. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

NEVADA: Reciprocity with oral examination, Aug. 5. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW MEXICO: Santa Fe, Oct. 7-8. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

OREGON: Basic Science, Portland, Oct. 26. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Written, Philadelphia and Pittsburgh, July 9-11. Bed-side, Philadelphia, July 12-13. Dir., Bureau of Professional Licensing, Dr. James A. Newpher, 358 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, Sept. 3. Sec., Dr. O. Costa Mandry, Box 3854, Santurce.

RHODE ISLAND: Providence, July 10-11. Sec., Division of Examination, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Rapid City, July 16-17. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

WASHINGTON: Basic Science, Seattle, July 11-12. Medical, Seattle, July 15-17. Sec., Department of Licenses, Mr. Nelson N. Vaughn, Olympia.

Colorado April Examination

Dr. Harvey W. Snyder, secretary, Colorado State Board of Medical Examiners, reports the written examination held at Denver, April 3-5, 1940. The examination covered eight subjects and included sixty-eight questions. An average of 75 per cent was required to pass. One candidate was examined and passed. One physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University at Illinois College of Medicine	(1936)	88.2
School	LICENSED BY ENDORSEMENT	Year Grad.	Per Cent
University of Nebraska College of Medicine	(1936)	N. B. M. Ex.

Ohio Reciprocity Report

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports twenty physicians licensed by reciprocity and two physicians licensed by endorsement on April 2, 1940. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Indiana University School of Medicine	(1920)	Indiana
State University of Iowa College of Medicine	(1936)	Iowa
University of Louisville School of Medicine	(1935), (1939, 2)	Kentucky
University of Michigan Medical School	(1931)	Michigan
Wayne University College of Medicine	(1939)	Michigan
St. Louis University School of Medicine	(1937, 2), (1938, 2), (1939, 2)	Missouri
Washington University School of Medicine	(1934)	Missouri

University of Nebraska College of Medicine.....	(1938)	Nebraska
New York University College of Medicine.....	(1931)	New York
University of Toronto Faculty of Medicine.....	(1936)	Michigan
Magyar Királyi Pázmány Petrus Tudományegyetem		
Orvosi Fakultása, Budapest.....	(1911)	New York
Université de Genève Faculté de Médecine....	(1935)	Maine, New York
School	LICENSED BY ENDORSEMENT	Year Endorsement
		Grad. of
Yale University School of Medicine.....	(1936)	N. B. M. Ex.
Boston University School of Medicine.....	(1937)	N. B. M. Ex.

Book Notices

Blood Transfusion. By Victor Horsley Riddell, M.D., F.R.C.S., Assistant Surgeon and Lecturer in Operative Surgery, St. George's Hospital, London. Cloth. Price, \$8. Pp. 370, with 65 illustrations. New York & London: Oxford University Press, 1939.

Here is an authoritative and thoroughly practical treatise on the practice of blood transfusion. While much has been written on this important subject, few sources of information will yield such a wealth of workable facts as this volume. The book reflects the author's intimate familiarity not only with the descriptive aspects of the subject but with practice as well. The material is particularly well organized and adequately illustrated. It is concisely presented without sacrificing clarity. All material extraneous to the practical phases of the subject has been purposely omitted. Although the author is English, he has traveled extensively in the United States and Canada and has managed to include the best practice current in this country as well as abroad. The material is distinctly cosmopolitan and carefully chosen. Technical details are explicitly given in a minimum amount of space. Each chapter is summarized and a current and pertinent bibliography is appended. The chapters on blood grouping technic, the universal donor, physiology of the blood groups and complications of blood transfusions are particularly well done. Few sources of information will yield as much fact in such a small space. The indications and contraindications to blood transfusion are clearly drawn and outlined. The information is direct and authoritative. The relative therapeutic values of whole and of citrated blood are discussed together with explicit directions for their use. The author candidly states that no reasonable or convincing evidence exists for therapeutic priority of either. Facts are dispassionately presented for each method. The chapter on apparatus is excellent and should prove invaluable to the physician as well as institutions. The chapter on stored blood embodies such experiences as the blood banks at the Cook County Hospital and at the Soviet blood transfusion institutes, and the use of cadaveric blood and placental blood. Limitations and virtues are discussed. The organization of a transfusion service and the subject of voluntary and professional donors are considered. This book deserves a place in every hospital and library. It is a working manual on the practice of blood transfusion pregnant with useful data and instruction. For a current comprehensive but concise treatise on this subject this textbook is preeminent. Every physician can purchase the volume with conviction that he has added something concrete to his working knowledge of medical practice.

Combined Textbook of Obstetrics and Gynecology for Students and Medical Practitioners. Revised and Rewritten by J. M. Munro Kerr, LL.D., M.D., F.R.F.P. & S., et al. Third edition. Cloth. Price, \$12. Pp. 1,192, with 499 illustrations. Baltimore: William Wood & Company, 1939.

The attempt of the nine authors to cover the subjects of obstetrics and gynecology in a single volume has been fairly well accomplished. It is natural, however, that a few subjects should receive scanty space. This is particularly true of operative gynecology and endocrinology. Only a total of thirteen pages is devoted to the three subjects "Ovulation and the Functions of the Ovary," "The Other Endocrine Glands" and "The Menopause." Surely in a book on obstetrics and gynecology containing a thousand pages more than thirteen should be devoted to the endocrine glands. The authors frequently refer to the use of intra-uterine douching, particularly for the removal of debris after an abortion and for stimulating uterine contractions during postpartum hemorrhage. In the United

States few obstetricians employ intra-uterine douches for any purpose. The authors believe that version (not followed by extraction) is the sheet anchor of the general practitioner faced with a grave case of placenta praevia. Nearly every patient who bleeds should be sent to a hospital, where far more satisfactory methods of treatment may be employed. Version through an incompletely dilated cervix in the presence of hemorrhage is a formidable and dangerous procedure. Even in the home the use of forceps on the baby's scalp as recommended by Willett and advocated also by the authors is far simpler and safer. For the low cervical operation the authors favor and illustrate the transverse incision in the lower uterine segment. They believe there is still a place for accouchement forcé or forcible dilation of the cervix followed by extraction of the child, especially when there is protracted labor caused by rigidity of the external os. For this purpose they mention the Bossi dilator, of which they say "Even when the greatest care is taken and the cervix very slowly stretched it is difficult to avoid doing serious injury. There is no place for this type of instrument." In spite of this statement, an illustration of the Bossi dilator is reproduced. Notwithstanding the number of men collaborating in the preparation of this book, the style is uniform throughout. The individual chapters, except two special ones, are not credited to individual authors. The illustrations are numerous and instructive but a large number were taken from other books. At least twenty-five are from Young's recent Textbook of Gynecology.

Arzt und Laboratorium: Die chemischen und mikroskopischen Untersuchungsmethoden und ihre Verwertung am Krankenbett. Von Dr. Hellmut Marx, Chefarzt der Inneren Abteilung der Krankenhäuser in Bethel bei Bielefeld. Boards. Price, 6 marks. Pp. 163, with 16 illustrations. Leipzig: Georg Thieme, 1939.

The purpose of this concise treatise is to describe briefly the most important laboratory methods that are of practical value in the practice of medicine. It is not a compendium of laboratory methods and makes no pretense at covering the field. The objective of the author apparently has been to select carefully those laboratory examinations which may be of distinct value to the practitioner in his daily work. The text contains chapters on urine examinations, kidney function test, gastric juice, bile, sputum, puncture fluids, basal metabolism determinations, blood chemistry and hematology. The chapter on blood chemistry and hematology occupies nearly half of the entire text. While this book has merit as a concise and current textbook of this subject, it is below the standard of similar books published in this country.

Pathology: An Introduction to Medicine and Surgery. By J. Henry Dible, M.B., F.R.C.P., Professor of Pathology in the University of London (The British Post-Graduate Medical School), London, and Thomas B. Davle, B.A., M.D., M.R.C.P., Professor of Pathology in the University of Liverpool, Liverpool. Cloth. Price, \$10. Pp. 931, with 374 illustrations. Philadelphia: Blakiston Company, 1939.

This textbook of pathology is a culmination of teaching effort in presenting the subject as "the grammar of medicine and surgery." The organization is different from many conventional works in that subdivisions into general and special pathology are not followed. Instead the first section of the book deals with inflammation, vascular disturbances, cellular damage and degenerations, disorders of growth and immunity. The succeeding section deals with special infections and anthrax, diphtheria and actinomycosis, which are discussed at some length as representative members of septicemic, toxemic and subacute inflammatory processes. Next the more common infections and virus diseases are discussed. The third section deals with systemic pathology. The arrangement of the book is distinctly peculiar to the system of pedagogy employed by the authors and is worthy of some reflection. The book is essentially a textbook written for students but can be profitably read by practitioners. The discussions are concise but adequate for an introductory course. The trend of the text is toward aiding the student to appreciate pathogenesis rather than the recognition of fixed morbid changes. The book is an excellent introduction to clinical medicine for this reason and should find favor with medical students in this country. It is written in an engaging literary style and represents a careful selection of subject material.

Anatomy and Physiology. By Frederic Theodore Jung, B.S., Ph.D., M.D., Assistant Professor of Physiology and Pharmacology, Northwestern University Medical School, Chicago, Anna Ruth Benjamin, B.A., M.D., Resident Physician, Elgin State Hospital, Elgin, Illinois, and Elizabeth Carpenter Earle, B.A., R.N., Educational Director, School of Nursing, St. Elizabeths Hospital, U. S. Department of Interior, Washington, D. C. Cloth. Price, \$3.50. Pp. 637, with 342 illustrations. Philadelphia: F. A. Davis Company, 1939.

This textbook for nurses incorporates many innovations which could be profitably utilized for other groups as well. It is distinctly an original presentation both in composition and in presentation. Many of the time honored pedantries traditionally found in a work of this type are refreshingly omitted. Pertinent facts are presented in a concise and interesting manner. Correlations between structure and function are expressed in the simplest possible terms, and at the end of each topic discussion the authors relate each part to the body as a whole. The entire text is well integrated and condensed to the greatest possible brevity. The book is attractively bound and the quality of paper and print is unusual for a textbook. The illustrations are plentiful and original and many of them are in four colors. The material is easily read in the two column pages. The book is of unusually high quality in every respect and should be warmly received as a textbook of unusually high merit by the nursing profession. It is distinctly an original presentation and the authors have made a distinct contribution to nursing education.

Pathogenic Microorganisms: A Practical Manual for Students, Physicians and Health Officers. By William Hallowell Park, M.D., and Anna Wessels Williams, M.D. Eleventh edition. Cloth. Price, \$8. Pp. 1,056, with 260 illustrations. Philadelphia: Lea & Febiger, 1939.

This book has long been regarded as a classic on its subject and will survive as a monument to Dr. Park, who died shortly after this revision was completed. This edition has been thoroughly revised and enlarged to include a section on bacterial variation and one on the metabolism of bacteria. The sections on pathogenic yeasts and molds, pathogenic protozoa and filtrable viruses have undergone complete revision. Other chapters have likewise undergone definite changes and additions. A number of prominent workers in special fields cooperated with the author to bring the material down to date in the usual authoritative manner that has always characterized this textbook. Not only do these additions make the work a rich source of information for medical students and laboratory workers, but the stress that has been given to problems of immunity, etiology and diagnosis of infectious diseases make it indispensable as a rich source of reference for the practicing physician. Few textbooks on this subject have the active collaboration of such authorities in their respective fields as this one. The changes in the new edition have been such that medical students, laboratory workers and libraries should have it in their possession. It is unquestionably the most current, concise, authoritative one volume textbook on bacteriology in any language.

Diseases of the Mouth. By Sterling V. Mead, D.D.S., B.S., M.S. Fifth edition. Cloth. Price, \$12.50. Pp. 1,059 with 696 illustrations. St. Louis: C. V. Mosby Company, 1940.

Apparently this is a popular textbook probably because of its inclusiveness, because of the liberal use of reproductions of well chosen roentgenograms, and because of the emphasis on diagnosis and treatment. It is largely limited to the field of minor oral surgery and related diseases, as reference to such matters as cleft palate, jaw resections and plastic operations is brief. Each chapter is followed by a generous bibliography. The present edition appears twelve years after the first. It and other late editions are characterized chiefly by progressive increase in size, as the defects and redundancies of the early editions persist. Of the ninety microscopic illustrations only about one third are worthy of inclusion or serve a useful purpose. Of the sixty-three colored plates, twenty-five could be discarded and not be missed. The legends are inadequate, incomplete and at times confusing, as that attached to figure 268 on page 473, which after long search is found to be connected with a case history on page 466. In figure 189 a protozoologist will no doubt locate the two amebas, but that is too much to expect of the general reader. It is suggested that the so-called pulp stones shown in figure 213 may be enamel drops, that a quart

or more of orange juice daily in the routine treatment of osteomyelitis or anything else is excessive and that the prognosis in agranulocytotic angina is not always bad. The text on the subject of dental caries illustrates a tendency of the author to handle a subject by the reproduction of numerous quotations from other authors without any attempt to weave them together logically by comment and discussion. This plan increases the size of the book without increasing its popularity. These serious faults detract from the advantages listed in the first sentence and greatly limit its usefulness.

Do You Want to Become a Doctor? By Morris Fishbein, M.D., Editor, Journal of the American Medical Association. Cloth. Price, \$1.50. Pp. 176. New York: Frederick A. Stokes Company, 1939.

As far as the practice of medicine is concerned, much has been said and little done about vocational guidance. The boy or girl contemplating a career in medicine has, at best, consulted a friendly physician but too often, without competent advice, has plunged headlong into the preparation for one of the most difficult and exacting professions. The author of this book has made available, in readily accessible form, a great deal of the information on which such a decision should be based. The opening chapters deal with medical education, its standards, costs and specific requirements, including the internship. Then follows a discussion of licensure and state examinations. Various phases of practice are described together with the ancillary vocations of various types of technicians. The closing chapters are devoted to the future of medicine and its relationship to society. Not the least illuminating to the neophyte are the admirably selected quotations portraying the life and character of the physician. Stevenson and Dean Inge, Percival and Sir William Osler, and many others, unite in expressing those ideals which have guided the medical profession and made it what it is.

Fuss und Bein: Ihre Erkrankungen und deren Behandlung: Ein Lehrbuch. Von Prof. Dr. med. Georg Hohmann, Direktor der Orthopädischen Universitäts-Klinik Frankfurt a. M. Third edition. Paper. Price, 26.34 marks. Pp. 462, with 405 illustrations. Munich: J. F. Bergmann, 1939.

The basic difference between this edition and others is the emphasis that is placed on the early recognition of abnormal and weak feet, and the recommendation of immediate treatment for the underlying mechanical condition. The author considers early treatment as part of the general education of the physiology of the body in order to prevent progression of abnormal foot conditions. In the last five years the shoe industry has made much progress. Orthopedic shoe makers are required to take special examinations and are educated scientifically from both theoretical and practical points of view. The shoe industry is cooperating with the orthopedic surgeons. The contents of the book include some excellent illustrations, line drawings and photographs. The subjects of clubfoot and deformities of the feet are omitted. The outline of the book and description of various conditions are interesting and stimulating to the orthopedic surgeon. The military point of view is emphasized. From the practical standpoint the book is helpful in diagnosis and treatment.

Surgical Applied Anatomy. By Sir Frederick Treves, Bart. Revised by Lambert Rogers, M.Sc., F.R.C.S., F.R.C.S.E., Professor of Surgery, University of Wales. Tenth edition. Fabrikold. Price, \$4.50. Pp. 748, with 192 illustrations. Philadelphia: Lea & Febiger, 1939.

This edition has been prepared by Prof. Lambert Rogers of the University of Wales. It constitutes a general revision of the ninth edition (edited by Prof. C. C. Choyce) with the addition of new material which has become available and applicable during the last five years. Mr. Rupert Parry and Mr. R. D. Owen have assisted in revision of the section on the eye, ear, nose and throat. The new material appears especially in the sections on cranial contents, on the neck and, to a less extent, in those on the orbit and eye and on the abdomen. The value of the book is sufficiently attested by its popularity for nearly sixty years. It was originally prepared by Sir Frederick Treves for students coming up for final English examinations in surgery. Students have found it an interesting and valuable indication of the clinical usefulness of anatomic facts, and practitioners have found it a valuable and reliable guide to clinical anatomy.

Rheumatism. By H. Warren Crowe, D.M., B.Ch., M.R.C.S., Senior Physician of the Charterhouse Rheumatism Clinic. Cloth. Price, 12s. 6d. Pp. 280, with 31 illustrations. London: John Bale Medical Publications Ltd., 1939.

This book was written entirely for the benefit of those who take an active part in the treatment of chronic rheumatic diseases and who are interested in the theory underlying modern technic and its practical application. The material is based on the experience of the author at the Charter House Rheumatism Clinic in London and his practice, limited entirely to rheumatic diseases. Experimental work carried out by the members of his staff has been included. The formation and progress of the Charter House Rheumatism Clinic are described. Dr. Crowe believes that all chronic rheumatic diseases are the result of the reaction of skeletal tissues to a foreign substance, the commonest of which is a bacterium of low virulence. The conclusions drawn are based on observation of more than 10,000 rheumatic cases extending over a period of thirty years. Vaccines are vigorously advocated. The chapters on roentgen therapy, orthopedic surgery, manipulation and physical therapy were written by specialists on the staff of the clinic.

Studies on Dysplastic Acetabula and Congenital Subluxation of the Hip Joint with Special Reference to the Complication of Osteo-Arthritis. By Gunnar Wlberg. Acta chirurgica Scandinavica Vol. LXXXIII, Supplementum LVIII. Paper. Pp. 135, with 52 illustrations. Stockholm: P. A. Norstedt & Söner, 1939.

This small monograph, written by one of Professor Waldenstrom's assistants, contains some interesting material on the anatomy and x-ray appearance of the normal hip. From his studies of hundreds of normal cases, the author evolved a method for determining whether the joint is normal or pathologic. He then examined many patients who had been roentgenographed during childhood so that a chronological study was possible. The author provides an elaborate description of methods of measuring to differentiate the normal from the abnormally developed acetabula. He discusses the connection between osteoarthritis with dysplastic acetabula and congenital subluxation of the hip. The section on arthrography is especially interesting.

The Life and Death Instincts (The Vita and the Fatum). By Arthur N. Foxe, M.D. Cloth. Price, \$2. Pp. 64. New York: Monograph Editions, 1939.

This small pamphlet is filled with a verbalistic juggling with the abstractions of psychoanalytic instinct theory. If Freud called his instinct theory "our mythology" this pamphlet deserves the name of "supermythology." It will be difficult for the reader to distinguish any logical connection between the different chapters which deal with such a broad variety of topics as the problem of criminality (the author calls it *criminosis*), the essence of life and death, fate (the author introduces a new expression *fatalisation*), chance and determinism, war and peace, and transference of the psychoanalytic process. The one connecting link between all this is generous references to Greek mythology. The clearest part of the pamphlet is the introduction, covering two pages.

Handbook of Orthopaedic Surgery. By Alfred Rives Shands Jr., B.A., M.D., Medical Director of the Nemours Foundation, Wilmington, Delaware. In collaboration with Richard Beverly Raney, B.A., M.D., Associate in Orthopaedic Surgery, Duke University School of Medicine, Durham, North Carolina. Second edition. Cloth. Price, \$4.25. Pp. 567, with 154 illustrations by Jack Bonacker Wilson. St. Louis: C. V. Mosby Company, 1940.

The first edition of this popular work, published in 1937, was well received. In the present edition there have been some definite changes. It is neater and more compact because of improvement in texture of paper, reduction in size of illustrations and deletion of unnecessary words and illustrations. There have been additions to the manuscript and illustrations in bringing the subject down to date. The illustrations, chiefly pen and ink drawings, contribute greatly to the value of the book. The bibliography, a valuable attribute of the volume, has been revised by addition of new material to July 1939. For purposes of classroom instruction there are twenty-four chapters of sound fundamental practical and theoretical orthopedic surgery. The views expressed are a combination of the best that can be obtained from the literature, textbooks and personal experience

of the authors. It is unnecessary to review the subject matter because it would be merely a review of the best opinions of orthopedic surgery in its entirety. This is probably the best book written purely as a handbook for orthopedic students and will continue to be popular in that role.

Recent Advances in Neurology. By W. Russell Brain, D.M., F.R.C.P., Physician in charge of Out-Patients to the London Hospital. Fourth edition. Cloth. Price, \$5. Pp. 364, with 24 illustrations. Philadelphia: Blakiston Company, 1940.

The publication of a fourth edition of this work within ten years indicates the widespread use and acceptance of this small volume. Brain assiduously has kept his editions modernized with alterations in the text and addition of new material. As a means of keeping abreast of progress in the field of organic neurology the work is excellent if used not as a textbook but as an initial point of reference.

Malyariya: Materialy k ucheniyu ob epidemologii i patogeneze. [By] F. M. Toporkov. [Epidemiology and Pathogenesis of Malaria.] Boards. Pp. 192, with 10 illustrations. Stalingrad: Oblastnoe Knigolzdatelstvo, 1939.

This small volume is concerned principally with statistical data on the incidence of malaria in the Union of Soviet Socialist Republics. The author suggests a program for a more effective control of both the epidemic and the endemic occurrence of the disease. No new or important observations are presented.

We Grow Up. By J. L. Kaukonen, Assistant Health Education Specialist, Federal Security Agency, U. S. Public Health Service. Educational Publication No. 3. Paper. Pp. 40, with illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1940.

This pamphlet is an education publication, highly artistic in its conception and exceedingly useful in the facts that it conveys. It is a book designed to educate the young about "the facts of life."

Nursing as a Profession. By Esther Lucile Brown. Second edition. Boards. Price, 75 cents. Pp. 157. New York: Russell Sage Foundation, 1940.

This edition follows the same general pattern as its predecessor and shares its values and limitations. Added material deals with the recommendations of the Interdepartmental Committee to Coordinate Health and Welfare Activities, the report entitled "Essentials of a Good Nursing School" and the recently revised Curriculum Guide for Schools of Nursing. Reference is also made to the activities of the Committee on Accrediting of the National League of Nursing Education. The author's question "Is Nursing a Profession?" remains unanswered.

Minlivist mikrobiv i bakteriofaglya (Trudi naukovoi konferentsii, Kiev, 1936). [Microbe variability and Bacteriophage (Papers of the Scientific Conference, Kiev, 1936).] Paper. Price, 22 krb. Pp. 488, with illustrations. Kiev: Ukr. SSR Academy of Sciences Press, 1939.

The volume is a collection of papers on the subject of microbe variability and bacteriophage presented at the scientific conference at Kiev in 1936 and published by the Academy of Sciences of Ukraine. It is a veritable encyclopedia of information on the subject.

Ten Years in the Congo. By W. E. Davis. Cloth. Price, \$2.50. Pp. 301. New York: Reynal & Hitchcock, 1940.

The modern medical missionary is a scientific adventurer. When Dr. Davis went into the heart of the Belgian Congo he carried drugs, surgical tools, medical ability, human kindness and a sense of humor. The story is therefore fascinating and should be an inspiration to the modern physician who finds the practice of medicine possible only with a retinue of assistants, technicians, hospitals and laboratories.

Zbirnik prats prisyvacheny pamyati akademika M. F. Mechnikova-Razvedenkova. Recueil de travaux dédié a mémoire de N. F. Mechnikov-Razvedenkov, membre de l'Académie des sciences. Paper. Price, 25 krb. Pp. 471, with illustrations. Kiev: L'Académie des sciences de la RSS d'Ukraine, 1939.

This is a memorial volume to Prof. N. F. Mechnikov-Razvedenkov, a prominent neuropathologist and member of the Academy of Sciences, who died on Dec. 20, 1937. The volume consists of thirty-three papers dealing with various clinical subjects. It does not lend itself to a review for THE JOURNAL.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Fracture of Mandible Resulting from Extraction of Impacted Molar.—The defendant dentists, Bloomenthal and Bennecke, on March 24, 1934, extracted the plaintiff's lower left third molar, which was impacted. After coming out of the anesthesia the patient suffered intense pain and a grating sensation when she attempted to move her jaw. After repeated requests during the next three days defendant Bloomenthal visited the patient on March 28 and again on March 30. She told him, so she said, about the pain, the grating sensation and the difficulty she experienced in opening her mouth. From March 31 to April 3 the patient visited the defendants several times at their offices and, as she stated, although she reiterated her complaints the defendants failed to do anything other than to administer mouth washes. On her next visit, April 4, eleven days after the extraction, the defendants caused roentgenograms to be taken for the first time. These roentgenograms and others taken later showed a fracture of the left side of the patient's mandible, but the defendants told her that the roentgenograms showed only "some sloughing of the bone" and "a sequestrum." She showed the defendants a piece of bone which she had removed from her mouth but they assured her that that "was perfectly natural." They did not immobilize her jaw in any way. About ten days after the extraction a paralysis of her left jaw developed associated with drooling of saliva. As her condition did not improve, on April 19 she consulted her family dentist, Dr. Nannestad, who took a roentgenogram which indicated to him "a complete fracture of the jaw." He sent her to Dr. Schaefer, an oral surgeon, to whom for purposes of interpretation the defendants had already shown their roentgenograms. Dr. Schaefer operated on her lower jaw, eurented the site of the extracted tooth and removed therefrom a piece of dead bone. Thereafter the patient improved steadily.

The patient sued the defendants for malpractice, alleging that they, incident to an unskillful extraction, broke her lower jawbone, failed to discover promptly the fracture and failed to treat the condition for some time, which negligence resulted in infection and improper closure of the teeth. A judgment of the trial court in favor of the plaintiff was reversed by the appellate court, first district, Illinois, holding that a verdict for the dentists should have been directed because the evidence was not sufficient to justify a judgment for the plaintiff. The plaintiff then appealed to the Supreme Court of Illinois.

At the trial a Dr. Remington, an orthopedic surgeon, testified that the roentgenogram taken by Dr. Nannestad on April 19 disclosed a "complete break" of the mandible. The fracture, he believed, should have been immobilized and failure to do so could cause both a "condition of anesthesia" in the jaw and malocclusion. A roentgenologist, Dr. Zeitlin, testified that this roentgenogram showed a "comminuted or complete fracture." Dr. Bernard, an oral surgeon, could find in the roentgenogram nothing to indicate a fracture. Bennecke testified that the roentgenograms taken by the defendants, which had been destroyed by a fire shortly after the suit was instituted, showed "a little crack there in the jaw . . . no appreciable separation of the bone, or anything of that sort." He admitted, however, that the roentgenogram taken by Dr. Nannestad did show a "comminuted fracture" of the mandible and that he treated the case as one of infection. Both defendants testified that their examinations revealed no displacement, malocclusion or crepitation. Dr. Schaefer testified for the defendants that when he first examined the plaintiff, about one month after the extraction, he found no marked displacement or malocclusion and nothing to indicate a fracture, and that he never detected any crepitation. His examination of roentgenograms revealed nothing to indicate a comminuted fracture of the mandible.

The patient contended that the trial court properly denied the defendants' motions for a directed verdict in their favor because

there was evidence to show that they concealed from her the fracture of her mandible and further that their failure to immobilize her jaw caused it to become malaligned and paralyzed. In passing on such a motion, said the Supreme Court, the evidence must be construed most favorably to the party adverse to it. Here the evidence so construed tended to show that prior to the extraction the patient's jaw was neither maloccluded nor paralyzed; that the defendants broke her lower jawbone during the extraction; that one of them, with reluctance, visited her at home; that eleven days after the extraction they took roentgenograms and, according to their own testimony, ascertained that she had a "cracked jaw" but did not so advise her; that the existence of a fracture of the mandible may be definitely determined by roentgenograms if it is completely broken through; that a roentgenogram taken April 19, before she received treatment by another dentist, disclosed a complete fracture; that the patient repeatedly told the defendants that she experienced a grating sensation when she moved her jaw; that a "cracked jaw," accompanied by a grating sensation, is indicative of a complete fracture; that the usual and accepted treatment for a complete fracture is immobilization, and that as a result of the defendants' failure to give or prescribe such treatment a permanent condition of malocclusion and paralysis of her jaw and chin developed. There was testimony, however, that the plaintiff's lower jawbone, if broken, was not a complete or comminuted fracture but merely an incomplete or partial one, and that if the latter condition existed the treatments given by the defendants were recognized as proper. Likewise, the defendants denied that the plaintiff ever complained to them about the grating sensation. On these and other factual questions the testimony was conflicting. The testimony of both defendants and of Dr. Schaefer, was, however, in accord that a "crack" in the plaintiff's mandible and a grating sensation when she opened her mouth, if those conditions were present, would indicate a complete fracture. Similarly the defendants and Dr. Remington and Dr. Schaefer agreed that a complete or comminuted fracture of the mandible would require immobilization. Regardless of the weight of the evidence, said the Supreme Court, the patient's evidence, standing alone, tended to show that the defendants did not use the skill and care in treating her after the extraction that dentists ordinarily use in similar circumstances and that she suffered permanent injury as a proximate result thereof. Accordingly, the Supreme Court held that the trial court's refusal to direct a verdict for the defendants was proper.

The Supreme Court did not agree with the defendants' contention that they had made only an erroneous diagnosis and were therefore not liable. The testimony tended to show more than a faulty diagnosis, namely, that the defendants knew that the mandible was "completely severed" but nevertheless they treated it as a "partially cracked jaw." Nor was there any question as to whether proper treatment had been given, since it was conceded that no treatment whatever was given or prescribed for a comminuted fracture.

The Supreme Court therefore reversed the judgment of the appellate court and remanded the cause to that court for further proceedings in accordance with the above opinion.—*Shutan v. Bloomenthal (Ill.)*, 20 N. E. (2d) 570.

Society Proceedings

COMING MEETINGS

- National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
- Pacific Northwest Medical Association, Spokane, Wash., July 10-13. Dr. C. W. Countryman, 407 Riverside Ave., Spokane, Wash., Secretary.
- Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
- Virginia Medical Society of, White Sulphur Springs, W. Va., July 29-31. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.
- Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
- West Virginia State Medical Association, White Sulphur Springs, July 29-31. Mr. Joe W. Savage, Public Library Bldg., Charleston, Executive Secretary.
- Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Digestive Diseases, Huntington, Ind.

7:189-226 (May) 1940

Extrarenal Azotemia in Gastrointestinal Hemorrhage: I. General and Clinical Consideration. D. H. Kaump, Temple, Texas, and J. C. Parsons, Des Moines, Iowa.—p. 189.

Id.: II. Experimental Observations. D. H. Kaump, Temple, Texas, and J. C. Parsons, Des Moines, Iowa.—p. 191.

Maximal Acidity of Intestinal Contents During Digestion. J. E. Thomas, Philadelphia.—p. 195.

*Acidity Modification Therapy in Peptic Ulcer. F. Steigmann and B. Fantus, Chicago.—p. 197.

*Secretory Studies in Whole Stomachs: Determination of Phenol Red in Gastric Contents. F. Hollander and A. Penner, with technical assistance of M. Saltzman and J. Glickstein, New York.—p. 199.

Use of Phenol Red as Dilution Indicator in Gastric Analysis. A. Penner, F. Hollander and A. Post, New York.—p. 202.

Psychic Gastric Secretion in Man. A. L. Bloomfield, San Francisco.—p. 205.

Studies in Human Biliary Physiology: IV. Comparative Effects of Orally Administered Olive Oil, Oleic Acid and Glycerin. With and Without Bile Salts, on Quantity of Bile Secretion. I. C. Zuckerman, M. Jacobi, B. Kogut and B. Klein, Brooklyn.—p. 208.

Some Remarks on Habitual Constipation and Related Nervous Disorders of Rectum. J. Bauer, New Orleans.—p. 210.

Volvulus of Stomach. R. Schatzki and F. A. Simeone, Boston.—p. 213.

Acidity Modification Therapy in Peptic Ulcer.—Steig-

mann and Fantus determined the antacid properties of four substances in the treatment of 100 patients with peptic ulcer. The substances were: (1) Sippy No. 1 powder (one part of calcium carbonate to three parts of sodium bicarbonate), (2) amphojel (a representative of the colloidal aluminum hydroxide group), (3) a neutralized karaya gum (representing the mucilaginous group) and (4) acid-bismuth mixture (a mixture of bismuth subnitrate and dilute nitric acid). All four antacids frequently produced relief of pain, but they often failed to produce a constant lowering of the free acidity. The acidity was lower in only 11 per cent of the cases after karaya, in 15 per cent after Sippy No. 1 powder, in 23 per cent after amphojel and in 18 per cent after the acid-bismuth mixture. It was higher than the control acidity in 21, 25, 16 and 14 per cent respectively. Sippy No. 1 powder produced complete neutralization for the duration of the test in 10 per cent of the cases and amphojel in 8 per cent. The Sippy powder, moreover, produced marked fluctuations and the greatest rise in the acidity. The fact that relief of pain is frequently obtained without definite or constant neutralization of acidity demonstrates that antacid action is not the sole factor responsible for the relief. Relief can most probably be explained on a lessening of gastric tension. The latter occurs whenever anything is placed in the stomach, probably explaining the beneficial results in the ulcer patients from the use of frequent meals alone. From the results of fractional aspirations in order to prevent the irritating effect of fluctuations in acidity, Sippy powder would have to be given at almost half hour intervals. Patients should do best on that medication which during the fractional test gives either continuously lower acidity or the least fluctuations in acidity in either direction. Ulcer therapy is not based solely on decreasing the gastric acidity.

Studies of Gastric Contents.—Hollander and his colleagues describe a method for the quantitative determination of phenol red concentration in specimens of human stomach contents which contain Liebig's extract, bile, mucin and other protein substances—such as would be obtained in the course of a gastric analysis in which phenol red is used as a dilution indicator. All interfering substances are removed adequately for colorimetry, without appreciable loss of the indicator. The reliability of the method was established on individual determinations of

108 mixed specimens, prepared with various proportions of a test meal containing 40 mg. of phenol red per liter. The standard deviation of this distribution was ± 0.22 mg. per liter. The mean error was ± 0.006 and the mode was -0.016 mg. per liter. Although the range of errors was -0.6 to $+0.9$, only four of the 108 error values were greater than ± 0.4 , or 1 per cent of the concentration of phenol red in the test meal.

American Journal of Orthopsychiatry, Menasha, Wis.

10:207-428 (April) 1940. Partial Index

What Constitutes Abnormality? I. S. Wile, New York.—p. 216.

Role of Visual Defects in Spelling and Reading Disabilities. G. Spache, New York.—p. 229.

Reading Failure and the Child's Security. Mary I. Preston, San Francisco.—p. 239.

Firesetting in Children. Helen Yarnell, New York.—p. 272.

The Psychology of Children Suffering from Organic Disturbances of Cerebellum. Lauretta Bender, New York.—p. 287.

Maternal Attitudes Found in Twenty-Five Cases of Children with Primary Behavior Disorders. Minna Field, New York.—p. 293.

Constructive Values Associated with Rejection. Mildred Burgum, New York.—p. 312.

Clinical Factor Influencing Variations in Intelligence Quotient. N. C. Kephart and A. A. Strauss, Northville, Mich.—p. 343.

Psychoanalytic Experiences in Public School Practice. H. Zulliger, Bern, Switzerland; translated by Gladys V. Swackhamer, Hartsdale, N. Y.—p. 370.

American Review of Tuberculosis, New York

41:531-674 (May) 1940

*Bronchiectasis: Study of Prognosis Based on Follow-Up of 400 Patients. K. M. A. Perry and D. S. King, Boston.—p. 531.

Beginning of Pulmonary Tuberculosis in Adults. H. Malmros and E. Hedvall, Lund, Sweden.—p. 549.

Primary Tuberculous Infection in Adults. H. Malmros and E. Hedvall, Lund, Sweden.—p. 562.

The Story of Tuberculin. H. S. Willis, Northville, Mich.—p. 573.

Tuberculosis Survey of Sugar Plantation in Hawaii. C. L. Wilbar Jr. and G. E. Wall, Ewa, Hawaii.—p. 582.

BCG Immunization: Comparison of Effects of BCG and of Heat Killed Organisms on Course of Subsequent Infection with Virulent Tubercle Bacilli in Guinea Pig. A. A. Liebow, C. G. Burn and W. B. Soper, New Haven, Conn.—p. 592.

Action of Serum, Cells and Blood on Acid-Fast Bacteria in Vitro: I. Absence of In Vitro Bactericidal Power Against Human Tubercle Bacilli or Timothy Bacilli in Serum-Leukocyte Mixtures or Blood of Normal and Immunized Rabbits. J. H. Hanks and B. Evans, Washington, D. C.—p. 605.

Id.: II. Failure to Demonstrate Bactericidal Power in Various Bloods: Relative Advantages of Solid Medium and of Liquid Blood in Demonstrating Viability of Bacilli in Blood. J. H. Hanks and B. Evans, Washington, D. C.—p. 620.

Id.: III. Evidence of Nutritional Basis of the So-Called Bactericidal Action of Rabbit Serum on Mycobacterium Phlei. J. H. Hanks and B. Evans, Washington, D. C.—p. 637.

*Guinea Pig Inoculation with Gastric Contents of Tuberculous Children. E. Rosencrantz and S. Hurwitz, San Francisco.—p. 645.

Bronchiectasis.—According to Perry and King, a follow-up of 400 cases of bronchiectasis under treatment at the Massachusetts General Hospital from 1926 through 1938 showed that in 49 per cent symptoms developed after acute respiratory infections. In 69 per cent the disease started in the first or second decade of life (42 per cent in the first and 27 per cent in the second). Three hundred and thirty-seven patients were traced; of these eighty-four were dead, 188 reported back to the hospital, sixty-five answered a questionnaire and of the sixty-three untraced patients a search through the death records in the Bureau of Vital Statistics showed that none had died in Massachusetts. There is a strong clinical impression that patients in whom bronchiectasis first develops before the age of 10 do not live beyond the age of 40. Statistical evidence supporting this impression is that only 9.4 per cent of the patients in whom bronchiectasis developed in the first decade lived to or are living at the age of 40 or more. Of the fifty-nine patients who reached the age of 40 or more only 15 per cent had their onset in the first decade. The disease may become sacellar or involve portions of the lung parenchyma, but it rarely spreads beyond the lobe or lobes originally involved. The mortality rate over a period of twelve years among the nonsurgically treated patients was 26 per cent; 41 per cent of them died within five years of the onset and 15 per cent lived twenty years or longer after the onset. Death of 78 per cent was a direct result of the disease. The mortality rate in the nonsurgical group among the male patients was 36 per cent as compared to 26 per cent among

the female patients. In the saccular type of bronchiectasis the mortality rate was 37 per cent as opposed to 13 per cent in the cylindric type. The operative mortality in 122 lobectomies performed on 116 patients was 3.3 per cent. The working and living capacity of the traced living patients was excellent in 67 per cent of the surgical group and in 38 per cent of the nonsurgical group. The mortality figures in the surgical and nonsurgical groups are not entirely comparable, but it is still evident that lobectomy is the treatment of choice, especially in unilateral disease. Nonsurgical treatment can be palliative only and preventive treatment is limited to measures directed toward reexpansion of collapsed lobes.

Inoculation of Gastric Contents in Diagnosis of Tuberculosis.—Rosencrantz and Hurwitz used the guinea pig (inoculation of gastric contents) method for the diagnosis of pulmonary tuberculosis among 169 consecutive children with positive tuberculin tests. Seventy-six, or 45 per cent, had tubercle bacilli in the gastric contents. Age was an important factor influencing the results. The results were positive in the nine patients up to 1 year of age. The younger the group, the higher were the percentages for bacilli in the gastric contents; the percentages decreased after the age of 5. This is explained by the fact that the tuberculous process in infants is still active and has not had time to heal and become encapsulated. Therefore children less than 2 years old with a positive tuberculin reaction should be considered as having active tuberculosis until proved otherwise by guinea pig inoculation. The incidence of positive observations in the gastric contents differs in the various clinical types of tuberculosis in children. The gastric contents gave positive reactions in all four cases of acute miliary tuberculosis. Among thirty-eight patients with primary pulmonary infiltration thirty-five, or 92 per cent, had tubercle bacilli. Seven of twelve children who had pleural effusion showed tubercle bacilli on lavage. Only seven of twenty-six children with primary tuberculosis with either the parenchyma or a hilus node calcified exhibited positive gastric lavages. Involvement of the hilus nodes alone was observed in sixty-six patients, and of these sixteen yielded tubercle bacilli. There were six cases of extrapulmonary tuberculosis (meningitis and osseous tuberculosis) and the tubercle bacillus was found in the gastric contents in each case. In all these cases x-ray evidence revealed pulmonary involvement, and the pulmonary tuberculosis was considered primary although the symptoms of the complications predominated. The method is of great importance, for in the absence of physical and x-ray signs it may be the only recognizable evidence of active tuberculosis.

Archives of Pathology, Chicago

29:589-740 (May) 1940

So-Called Mixed Tumors of Mammary Gland of Dog and Man, with Special Reference to General Problem of Cartilage and Bone Formation. A. C. Allen, New York.—p. 589.

*Evaluation of Apparently Increased Incidence of Primary Carcinoma of Lung. T. M. Peery, Washington, D. C.—p. 625.

Experimental Studies in Cardiovascular Pathology: I. Pathologic Changes in Organs of Rats Produced by Chronic Nitrite Poisoning. W. C. Hueper and J. W. Landsberg, New York.—p. 633.

*Incidence of Primary Carcinoma of Lung: Review of Yale Autopsy Protocols, 1917 to 1937. P. D. Rosahn, New Haven, Conn.—p. 649.

Dissecting Aneurysm of Aorta in Experimental Atherosclerosis. T. Leary and S. Weiss, Boston.—p. 665.

Behavior of Tubercle Bacilli Following Their Intravenous Injection into Resistant Animal (Rat). N. C. Oswald, New York.—p. 678.

Primary Carcinoma of Lung.—Peery suggests that statistics on the probable increase of primary carcinoma of the lung are misleading for the following reasons: 1. Prior to 1900 primary carcinoma of the lung was probably diagnosed less frequently than it actually occurred because of the belief that the tumor was exceedingly rare. Most of the tumors of this type were considered metastatic, probably erroneously. 2. Possibly the diagnosis of pulmonary cancer is now made more frequently than is justifiable. Involvement of the bronchial mucosa is not a reliable criterion as metastases to the bronchial mucosa are relatively common. The success of surgical operation and of the application of radium and x-rays in eliminating accessible primary growths, while the secondary tumors remain viable and growing, places an obligation on the clinician and the pathologist to evaluate carefully the changes in every

case. 3. The abandonment of the diagnoses "endothelioma of the pleura," "oat cell tumor of the mediastinum" and "tumor of the superior pulmonary sulcus" and the placing of these tumors in the classification of primary carcinoma of the lung, have enlarged the group considerably. These tumors appear to the author to be correctly classified as primary carcinoma of the lung, but the change has swollen the statistics rather than increased the incidence of the disease. Undoubtedly primary carcinoma of the lung is quite common, but apparent increase in its incidence should not be accepted as an actual increase until due allowances are made for the pendulum to come to rest.

Incidence of Primary Carcinoma of Lung.—Rosahn presents new data which show that the increase in the incidence of carcinoma of the lung is not only apparent but real. Among 4,114 persons examined post mortem from Sept. 22, 1917, to Dec. 31, 1937, only 2,968 of whom were more than 20 years of age, 435 carcinomas were found in 425 persons. From 1917 to 1927 there were ten primary pulmonary tumors, or 7.35 per cent of the 136 carcinomas encountered during this period. This compares with thirty-three primary pulmonary cancers seen from 1928 to 1937, or 11.04 per cent of the 299 cancers observed. From 1917 to 1927 carcinoma of the lung was the fifth most frequent tumor. In the following decade it rose to second place. With the exception of prostatic carcinoma, carcinoma of the lung was the only one to increase appreciably during the second of the two ten year periods under consideration. The increasing incidence of primary cancer of the lung is further enhanced by the demonstration that it alone of all tumors had a significant positive raising trend. Analysis of certain factors (improved clinical and pathologic methods of diagnosis, increased attention to this neoplasm, increase in the span of human life and no comparable increase in cutaneous tumors), often cited as evidence that cancer of the lung has shown only a relative increase, has exerted little or no influence on the statistically significant increase in primary carcinoma of the lung found at necropsy in the New Haven Hospital, and it is concluded that the observed increase is real and absolute. Indirect evidence appears to justify the additional conclusion that the real increase in primary carcinoma of the lung observed in this postmortem material is characteristic also of the population at large.

Journal Industrial Hygiene & Toxicology, Baltimore

22:157-198 (May) 1940

Serial Chest Roentgenograms of 3,179 Office Employees, 1926-1938. H. H. Fellows, New York.—p. 157.

Dermatitis from Cashew Nut Shell Oil. J. G. Downing and S. W. Gurney, Boston.—p. 169.

Ventilation of Trichlorethylene Degreaser. W. N. Witheridge and H. T. Walworth, Detroit.—p. 175.

Field Determinations of Carbon Disulfide in Air. F. J. Viles, Boston.—p. 188.

Journal of Lab. and Clinical Medicine, St. Louis

25:669-778 (April) 1940. Partial Index

Distribution of Free and Conjugated Sulfanilamide and Sulfapyridine Between Corpuscles and Plasma in Both Human and Rabbit Blood. L. Hansen, Philadelphia.—p. 669.

Note on Level of Glucose and of Nonfermentable Reducing Substances in Therapeutic Insulin Shock. W. H. Forbes and T. Czarski, Baltimore.—p. 679.

Effect of Sulfanilamide on Cross Matching of Blood: Preliminary Report. S. Kreinin, Brooklyn, with technical assistance of Frances A. Hamblen and Lucy Porcelli.—p. 690.

Protection Against Rabies: I. Effect of Frequency of Dosage of Vaccine on Immunity. J. M. Moss, Indianapolis.—p. 702.

Transfusion of Blood from Artificially Immunized Donor in Treatment of Chronic Bacillary Dysentery. R. Turell, New York.—p. 706.

Animal Tissue Reaction to Particulate Copper Stearate. P. T. Knies, Columbus, Ohio.—p. 726.

Distribution of Sulfanilyl-2-Aminopyridine in the Body. H. Chinn and J. Bellows, Chicago.—p. 735.

I. Studies of Liver Function in Health and Disease: Observations on Simple and Accurate Method for Quantitative Determination of Bile Salts in Urine and Bile. L. M. Morrison and W. A. Swalm, Philadelphia.—p. 739.

Tolerance of Diabetic Persons for Dextrose During Various Times of the Day. M. Wishnofsky, A. P. Kane, W. C. Spitz and C. S. Byron, Brooklyn.—p. 754.

Difficulties Encountered in Test for Standardization of Toxin Used Against Scarlet Fever. Betty S. Kolchin, New York.—p. 762.

Journal of Nervous and Mental Disease, New York 91:557-696 (May) 1940

- Colloid (Paraphysial) Cyst of Third Ventricle with Rupture Into Caudate Nucleus and Internal Capsule. C. P. Larson, Fort Steilacoom, Wash.—p. 557.
- Regression in Catatonia. G. S. Sprague, White Plains, N. Y.—p. 566.
- Beriberic Neuromyoseloses. A. Austregesilo, Rio de Janeiro, Brazil.—p. 579.
- A Genetic Approach to the Problem of Stammering. A. B. Berman and G. J. Train, Brooklyn.—p. 590.
- Progressive Facial Hemiatrophy: Report of Case with Attacks of Syncope and Gynandromorphism. M. O. Wolfe and M. L. Weber, Dearborn, Mich.—p. 595.
- Heredopathic Combination of Congenital Deformity of Nose and of Myoclonic Torsion Dystonia. L. Benedek and E. Rakonitz, Budapest, Hungary.—p. 608.
- Studies in Delayed Awakening in Insulin Shock Therapy (Sakel): II. Blood Pressure Observations and Their Possible Interpretation. G. W. Robinson and G. W. Robinson Jr., Kansas City, Mo.—p. 625.

Journal of Neurophysiology, Springfield, Ill. 3:191-282 (May) 1940

- Electric Responses Derived from Superior Cervical Ganglion with Micro-Electrodes. P. O. Therman, A. Forbes and R. Galambos, Boston.—p. 191.
- Effect of Cortical Lesions on Affective Pupillary Reactions. B. Ury and E. Oldberg, Chicago.—p. 201.
- Postural Reflexes and Grasp Phenomena in Infants. B. L. Pacella, Brooklyn, and S. E. Barrera, New York.—p. 213.
- Action of Ether and Nembutal on Nervous System. P. Heinbecker and S. H. Bartley, St. Louis.—p. 219.
- Degeneration and Regeneration of Sympathetic Synapses. W. C. Gibson, Oxford, England.—p. 237.
- Studies of Motor Performance After Parietal Ablations in Monkeys. Margaret A. Kennard and M. M. Kessler, New Haven, Conn.—p. 248.
- Somatic and Autonomic Reflexes in Spinal Monkeys. A. L. Sabs and J. F. Fulton, New Haven, Conn.—p. 258.
- Nerve Activity Accompanying Fasciculation Produced by Prostigmine. R. L. Masland and R. S. Wigton, Philadelphia.—p. 269.
- Effects on Respiration, Blood Pressure and Gastric Motility of Stimulation of Orbital Surface of Frontal Lobe. P. Bailey and W. H. Sweet, Chicago.—p. 276.

Maine Medical Association Journal, Portland 31:115-150 (May) 1940

- Medicine Today. L. P. Gerrish, Lisbon Falls.—p. 115.
- Nature of Neuroses. M. Marquardt, Augusta.—p. 118.
- Cardiac Emergencies and Their Treatment. G. R. Brow, Montreal.—p. 122.
- One Thousand Tuberculin Tests with Purified Protein Derivative. E. A. Greco and Mary G. Gordon, Portland.—p. 128.

Missouri State Medical Assn. Journal, St. Louis 37:189-232 (May) 1940

- Cancer of Uterus: Early Diagnosis and Treatment. G. D. Royston, St. Louis.—p. 189.
- Underwater Therapy in Chronic Arthritis. V. E. Frazier, Kansas City.—p. 192.
- Fractures of Vertebrae During Metrazol Therapy. L. L. Tureen and J. A. Key, St. Louis.—p. 194.
- Value of Electrocardiogram in Diagnosis. G. Asher, Kansas City.—p. 197.
- Syphilitic Cardiovascular Disease. C. C. Dennie, Kansas City.—p. 198.
- Pericarditis. R. E. Myers, Joplin.—p. 200.
- Coronary Artery Disease. H. M. Parker, Kansas City.—p. 202.
- *Beverage Alcohol and Heart Disease. F. C. Helwig, Kansas City.—p. 204.
- Functional Heart Disease. W. M. Kinney, Joplin.—p. 206.

Beverage Alcohol and Heart Disease.—Helwig believes that alcohol by itself is of no significance in the etiology of angina pectoris, essential hypertension, arteriolonephrosclerosis and coronary sclerosis. There is considerable evidence to show that it may have a definite retarding effect on the development of arteriosclerosis and atherosclerosis. It has been stated that alcohol may be of extreme benefit in coronary disease. According to Paul White 1 or 2 ounces (30 or 60 cc.) of whisky, brandy or rum may give relief from angina pectoris within a few minutes. There is no clinical or pharmacologic evidence that would suggest that alcohol alone ever produces heart disease. The symptoms may be produced by a deficient diet in the absence of alcohol, and often they may take place long after the ingestion of alcohol has ceased. The mere fact that symptoms such as polycytemia, pellagroid lesions and cardiovascular dysfunction disappear on continuous alcoholic intake with simultaneous administration of vitamin B should make it obvious that alcohol can be only a factor. Pellagra and various types of cardiac disease are known to be associated with specific avitaminosis without alcoholism and will clear up in addicts with proper

vitamin therapy in the face of continued alcoholism. Patients with acute and chronic alcoholism and heart disease should be subjected to an extremely critical and searching analysis of their previous dietary habits before a conclusion regarding the etiologic background of the cardiac condition is reached. "Beer drinker's heart" is an obsolete term and should be abandoned.

Northwest Medicine, Seattle 39:157-198 (May) 1940

- Lipiodol versus Air as Aid in Diagnosis of Protrusion of Intervertebral Disk. S. N. Berens, Seattle.—p. 160.
- Vitallium in Internal Fixation in Bone Surgery. J. I. Tuell, Seattle.—p. 163.
- Ununited Fractures of Both Bones of Forearm. E. LeCocq, Seattle.—p. 165.
- Gibney Dressing for Sprained Ankle. H. E. Allen, Seattle.—p. 166.
- Treatment of Hallux Valgus. W. Kelton, Seattle.—p. 167.
- Treatment of Suppurative Arthritis. D. G. Leavitt, Seattle.—p. 169.
- Diagnosis and Treatment of Acute Osteomyelitis. J. F. LeCocq, Seattle.—p. 171.
- Gastrojejunocolic Fistula: Report of Case. P. C. Gunby, Seattle.—p. 173.
- Enterovesical Fistula. R. D. Forbes, Seattle.—p. 174.
- Sliding Hernia. O. F. Lamson, Seattle.—p. 175.
- Miller-Abbott Intestinal Intubation: Evaluation in Treatment of Intestinal Obstruction. J. Duncan, Seattle.—p. 177.
- Exclusion Operation for Carcinoma of Colon. W. C. Speidel, Seattle.—p. 179.
- Ovarian Cysts Complicating Pregnancy. C. M. Helwig, Seattle.—p. 180.
- Female Pseudohermaphroditism. P. R. Rollins, Seattle.—p. 181.
- Convulsions Associated with Nitrous Oxide-Ether Anesthesia. W. B. Cook, Seattle.—p. 182.

Texas State Journal of Medicine, Fort Worth 36:1-70 (May) 1940

- Bone Disease in Children: Radiologic Features. J. B. Johnson and H. M. Anspach, Galveston.—p. 5.
- Id.: Orthopedic Features. G. W. N. Eggers, Galveston.—p. 7.
- Surgical Treatment of Uterovaginal Prolapse. L. W. Pollok, Temple.—p. 15.
- Treatment of Infections of Prostate Gland. J. R. Nicholson, San Antonio.—p. 19.
- Weltmann Reaction in Malignant Disease. A. B. Cairns and Luise Brandenstein, Dallas.—p. 22.
- Observations on Etiology of Polycythemia Vera. W. B. Adamson and J. E. Storey, Abilene.—p. 26.
- Cutaneous Precancerosis. L. E. Edens, Austin.—p. 29.
- A Pioneer Texas Emasculator: Chapter from the Life of Dr. Gideon Lincecum. P. I. Nixon, San Antonio.—p. 34.
- We Medical Students. J. W. Spies, Galveston.—p. 38.
- Study of Hypopyon Ulcer of Cornea. B. B. Hutchinson, Lubbock.—p. 40.
- Expanding Field of Public Health Activities. J. N. Baker, Montgomery, Ala.—p. 43.
- New Developments in Crippled Children's Work. J. J. Brown, Austin.—p. 47.

Virginia Medical Monthly, Richmond 67:261-326 (May) 1940

- Largest Collection of Medical Literature Ever Assembled: Story of the Army Medical Library, with Notes of Virginians Who Have Directed It. E. E. Hume, Carlisle, Pa.—p. 261.
- Remarks on Diagnosis and Treatment of Angina Pectoris. E. G. Scott, Lynchburg.—p. 273.
- Esophageal Diverticulum. R. L. Payne and R. D. Jones Jr., Norfolk.—p. 278.
- Treatment of Sciatica. D. M. Faulkner, Richmond.—p. 287.
- Experience with Thyroid Disease in Western Virginia. R. P. Bell, Staunton.—p. 293.
- Endocrinology Briefs: Ovaries. J. P. Lynch, Richmond.—p. 296.
- Use of Unna's Paste in Treatment of Varicose Ulcer. W. B. Marbury and R. L. Jackson, Washington, D. C.—p. 298.
- Analysis of Cesarean Section at University of Virginia Hospital. J. M. Nokes, University.—p. 300.
- Lithopedion with Calcified Placenta: Case Report. P. W. Oden and H. C. Lee, Richmond.—p. 304.
- Sulfanilamide in Burns. B. C. Grigsby, Bonny Blue.—p. 306.

West Virginia Medical Journal, Charleston 36:193-240 (May) 1940

- Function of Joints in Relation to Fracture Treatment. R. H. Kennedy, New York.—p. 193.
- Role of Psychiatry in Pediatrics. J. Basman, Charleston.—p. 199.
- What May Be Seen in the Eyes. R. A. Tomassene, Wheeling.—p. 202.
- Progress in Orthopedic Surgery, with Discussion of Some of the Newer Principles of Treatment. A. R. Lutz, Parkersburg.—p. 205.
- Probable Effects of Testosterone on Prostatic Hypertrophy. C. J. Reynolds, Bluefield.—p. 211.
- Some Diseases of the Mouth. C. W. Stuart, Chicago.—p. 215.
- Surgical Problem of Gallbladder Disease. L. Gage, Princeton.—p. 220.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

1:719-756 (May 4) 1940

- Insulin Deficiency and Insulin Inefficiency. H. P. Hinkworth.—p. 719.
Strain Variations in Resistance of *Streptococcus Viridans* to Sulfonamide Compounds. R. H. A. Swain.—p. 722.
Splinting Fractures of Humerus. K. O. Parsons and A. T. Hart.—p. 726.
Diphtheria Prophylaxis: Optimal Dosage and Technique in Use of Alum Precipitated Toxoid. J. T. Lewis.—p. 728.
Benzedrine Sulfate: Its Use to Interrupt Avertin Anesthesia. J. Lloyd.—p. 729.

Journal of Physiology, Cambridge

98:1-140 (March) 1940. Partial Index

- Glycogen and Calcification. G. E. Glock.—p. 1.
Effect of Temperature on Mechanical Response and Viscosity and Oxygen Consumption of Unstriated Muscle. M. Sadashiva Rao and I. Singh.—p. 12.
Composition of Alveolar Air. I. F. S. Mackay.—p. 73.
Effect of Gravity on Blood Pressure of Cat. O. G. Ebbelun.—p. 79.
Renal Excretion of Inulin and Creatinine by Anesthetized Dog and Pnump-Lung-Kidney Preparation. J. A. Shannon and F. R. Winton.—p. 97.
Inactivation of Adrenalin by Phenolases. H. Maschko and H. Schlossmann.—p. 130.

Lancet, London

1:819-864 (May 4) 1940

- Death in the First Month and the First Year. C. McNeill.—p. 819.
Treatment of Certain Types of External Hemorrhoids. C. P. G. Wakeley.—p. 822.
Lumbar Curve in Women: Changes Produced by Displacement of Center of Gravity. L. K. Klinderová.—p. 827.
*Insulin Suppositories. H. Braun.—p. 829.
*Subendocardial Hemorrhages in Shock. H. L. Sheehan.—p. 831.
*Wounds of Chest Treated by Artificial Pneumothorax. C. H. Kreiselmair.—p. 832.

Insulin Suppositories.—Braun points out that insulin introduced into the rectum is destroyed by the tryptic digestive ferments. His object was to protect the insulin against these ferments, which can act in an alkaline medium only, by adding acids to it and to accelerate its absorption by adding substances which increase the surface tension. Suppositories of theobroma oil were used as the vehicle for these substances. The tests were carried out on rabbits and on healthy human beings. The blood sugar estimations were made by the Hagedorn-Jensen method at intervals of from fifteen to thirty minutes, beginning from thirty to forty minutes after the introduction of the suppository. About 150 tests on rabbits and as many on human beings were carried out. Suppositories consisting of theobroma oil and insulin had no effect on rabbits or on man. The addition of acid preserved the efficacy of the insulin in suppositories of theobroma oil. A combination of lactic and palmitic acid proved most effective. However, since palmitic acid melts only at 60 C., it was necessary to melt it first with theobroma oil in the proportion of 15 to 85; this yielded a mixture with a melting point of 33 C. The addition of saponin increased the intensity and duration of the action of an acid-containing insulin suppository in rabbits and man. The action of insulin introduced into suppositories sets in soon and attains its maximum after thirty to forty minutes, at the end of which time the action again subsides rapidly. Larger doses of insulin increase not only the intensity but also the duration of the action. The effect of insulin suppositories may be varied by increasing the insulin content in an otherwise unchanged combination, by modifying the quantity of acid and saponin without changing the amount of insulin or by varying the quantity of each substance. Wuhrmann tested insulin suppositories clinically and found them to be of value (*Schweiz. med. Wchnschr.* 69:787 [Sept. 2] 1939; abstr. *THE JOURNAL*, Nov. 11, 1939, p. 1844).

Subendocardial Hemorrhages in Shock.—Sheehan asserts that subendocardial hemorrhages are among the most regular pathologic aspects of shock due to obstetric causes. The material reviewed is from the routine obstetric necropsies performed in the Glasgow Royal Maternity and Women's Hospital during the last two and a quarter years in which a systematic search

for the hemorrhages was made in every case. Shock resulted from the usual obstetric causes: dystocia in sixteen cases, retained placenta in twelve, uteroplacental apoplexy in nine, rupture or inversion of the uterus in five, and other conditions, including those in which hemorrhage played some part, in ten. Subendocardial hemorrhages, localized to the left side of the interventricular septum and less often also to the muscular papillares and trabeculae of the left ventricle, are almost invariably present in obstetric deaths from shock, except when the patient dies rapidly, that is within an hour. The author thinks that subendocardial hemorrhages cannot be considered as merely one aspect of generalized damage to the capillaries. They are not to be confused with the widespread hemorrhages in mucosae and serosae, which some authors record in animal experiments but which have not been found in these cases of shock in human beings. They cannot be dismissed as "agonal lesions" which may occur in any kind of death; on the contrary, they are restricted to certain special types of death. The close relationship between their incidence in cases of shock and the duration from the onset of shock to the time of death suggests that they usually take some time to develop. In postmortem examination on patients who die some days after recovery from shock there are usually no remaining lesions, or, if present, they are quite small. It appears, therefore, that the hemorrhages take place not in the lesser degrees of shock but only in severe or fatal cases. The fact that they are also found in deaths from various kinds of cerebral lesions suggests a possible nervous mechanism for their production in shock. They are presumably a post-mortem indication that a vascular disturbance in this region has been present for some time before death, but the relationship of this vascular disturbance to the syndrome of shock is not yet elucidated.

Wounds of Chest Treated by Artificial Pneumothorax.—According to Kreiselmair, the treatment of chest wounds by artificial pneumothorax was introduced into the Italian army in 1916 by Morelli. During the Spanish war the author saw death from intrathoracic hemorrhage after a comparatively small chest wound. Hemorrhage is intensified or prolonged by the negative pressure in the pleural cavity. The hemothorax does not check the hemorrhage, for if the wound is in the upper part of the lung the hemothorax does not reach the level of the wound. Spontaneous cessation of pulmonary hemorrhage is more probably due to the pneumothorax which usually accompanies penetrating wounds of the chest. A traumatic pneumothorax is not an indication for operation unless it is valvular or complicated by an infected effusion or by progressive hemorrhage from the lung. When there is progressive pulmonary hemorrhage, and when there are foreign bodies in the lung, a complete artificial pneumothorax should be induced to cause collapse of the lung. The hemothorax, if large, should be cleared out by thoracocentesis as completely as possible, because its absorption takes a long time, causes thickening of the diaphragm and pleural adhesions, and impedes the cardiac action and the expansion of the sound lung, and there is a risk of pyopneumothorax with a doubtful prognosis. The artificial pneumothorax has its therapeutic effect on the wound of the lung, stops or reduces the hemorrhage from the lung, prevents the obliteration of the sinuses and the formation of adhesions between the visceral and parietal pleura, protects the lung from further damage due to movement of foreign bodies and prevents inflammation of the lung caused by these foreign bodies. Artificial pneumothorax therefore should have a permanent place in thoracic surgery, especially in war time.

Practitioner, London

144:453-548 (May) 1940

- Pleisy and Allied Disorders. W. H. Wynn.—p. 453.
Treatment of Ashtma. J. N. Cruickshank.—p. 465.
Problems of Pulmonary Tuberculosis in the Adolescent. W. E. Lloyd.—p. 478.
Industrial Lung Disease: Diagnosis and Treatment. H. H. Moll.—p. 487.
Diagnosis and Treatment of Enlarged Mediastinal Glands in Children. P. Williams.—p. 499.
Prescribing in Wartime. H. N. Linstead.—p. 506.
Modern Therapeutics: XI. Diuretics and Urinary Antiseptics. E. B. Mayrs and T. H. Crozier.—p. 516.

Presse Médicale, Paris

48:361-384 (April 10-13) 1940.

Effect of Chronic Intoxication with Chlorine Impregnated Atmosphere on Experimentally Induced Tuberculosis of Guinea Pig. F. Arloing, E. Berthet and J. Viallier.—p. 361.
Collective Oxygen Inhalators Fed by Liquid Oxygen. Cot and Genaud.—p. 361.

Angina Pectoris Due to Thyroid Dysfunction. J.-C. Mussio-Fournier and J.-T. Fischer.—p. 363.

Late Relapses in Unilateral Tuberculous Cavities Apparently Healed by Thoracoplasty. A. Bernou, H. Fruchaud and M. Gautier.—p. 366.

Late Relapses After Thoracoplasty.—Bernou and his associates report twenty instances (8.26 per cent) of late recurrence after 242 thoracoplasties performed for unilateral pulmonary cavities. In three of the twenty cases the contralateral lung showed involvement, in seven surgical intervention was not extensive enough and in the other ten pulmonary collapse had been unsatisfactory. Seven of the patients made a good recovery after subsequent management with rest and rib resection on a larger scale. Only four of the ten patients were regarded by the authors as offering a doubtful prognosis because of weak walls after extraperiosteal resection. Observation time extended from fifteen months to eight years for the group of cases of severe late reactivation and from seven to sixteen months for the group in which thoracoplasties were performed with extraperiosteal resection with deficient wall collapse. Relapses were noted in 3.7 per cent of the cases presenting subperiosteal resection in which the field of operation had been unduly narrowed. A 30.8 per cent reactivation of infection was noted in thoracoplasty with extraperiosteal resection showing too rapid a recovery. In apparently healed pulmonary lesions subsequent trauma caused to the sensitive lung by effort or cough may reactivate former lesions. No relapse occurred in any of 242 cases at the site of the primary lesion or directly under it when surgical intervention was carried out effectively with proper parietal collapse.

Revue Belge des Sciences Médicales, Louvain

12:1-32 (Jan.) 1940

Circulatory Inversion in Kidney. E. Lauwers.—p. 1.

*Adeno-Acanthoma of Cervix Followed Two Years Later by Papilliferous Adeno-Epithelioma of Uterus: Case. P. Desaiue.—p. 12.
Acromegaloïdism in Puberty: Case. M. Schachter.—p. 24.

Adeno-Acanthoma of Cervix and Adeno-Epithelioma of Uterus.—Desaiue discusses a case in which an adeno-acanthoma of the cervix was followed two years later by an adenocarcinoma of the uterus, the two neoplasms disclosing differentiated microscopic pictures. The patient, 44 years old, with a normal history, presented a cervical tumor which was successively treated with radium (vagina, intra uterum) and roentgen rays. She remained in excellent health until, a few years later, a true papilliferous adeno-epithelioma of the uterus was diagnosed. Hysterectomy was performed, which left her apparently in perfect health. The author believes that the two tumors belong to the category of multiple growths and arose independently of each other. The effect of the roentgen rays in canceration of tissue is not excluded. Diagnosis and biopsy should not confine themselves to the cervix, even if this alone is affected, but include more extensive examinations of the uterine area. Hysterectomy is the method of choice. If irradiation is employed, it should induce a complete and permanent atrophy of the mucosa of the uterus.

Chirurg, Berlin

12:145-176 (March 15) 1940. Partial Index

Care in Base Hospital for Persons Injured by Bombs: Experiences in China. C. Reimers.—p. 145.

Treatment of Injuries of Male Urethra. F. Voelcker.—p. 152.
Preparatory and After-Treatment of Patients Operated on for Rectal Cancer. H. H. Westermann.—p. 156.

*Digitalis in Treatment of Wounds. H. Baron.—p. 160.

Digitalis in Treatment of Wounds.—Baron studied the effect of digitalis on wounds, particularly on those failing to respond to the customary treatments. Digitan was applied either in a 10 per cent solution or as a 10 or 20 per cent ointment. A compress saturated with the solution is placed on the wound and a layer of cotton saturated with the solution placed over it. This dressing is changed after twenty-four hours. Zinc paste

is applied to the surrounding healthy tissue to prevent maceration. Digitan ointment is used first in the stronger and later in the weaker concentration. Ointment bandages, changed daily, were employed in the treatment of new, extensive burns. The ointment is especially advantageous in facial burns because it is odorless. Ointment bandages, remaining in place for about a week, were applied to wounds that had improved under digitan compresses. Digitan ointment bandages in combination with plaster of paris casts were left in place for several weeks. This therapy has been employed in forty-eight cases, including post-operative and post-traumatic suppurating wounds, burns, carbuncles, crural, decubital and x-ray ulcers, necrosis caused by contrast medium and osteomyelitis. The advantages of digitalis treatment of wounds are: 1. It improves blood perfusion and purification of wounds. 2. It inhibits inflammation and stimulates granulation. 3. It stimulates epithelization. The author suggests that these effects are the result of improved blood flow in the capillaries of the wound brought about by the action of digitalis on the cells of the capillary wall. A bactericidal effect is probable but has not been definitely proved.

Deutsche medizinische Wochenschrift, Leipzig

66:281-308 (March 15) 1940. Partial Index

*Treatment of Acute Lobar Pneumonia with Sulfapyridine: Report of 303 Cases. C. Hegler.—p. 281.

Comparative Investigations on Action of Various Disepsants (Sulfanilamides) in Treatment of Gonorrhea. H. Löhe and R. Wawersig.—p. 283.

Chemotherapy in Gynecology. W. Stoeckel.—p. 286.

Treatment of Rheumatism with Radium Irradiations. Stoia and Heda Stoia.—p. 291.

Sulfapyridine in Acute Lobar Pneumonia.—Hegler reports 303 cases of acute lobar pneumonia treated with sulfapyridine. The initial dose was 2 Gm. Nausea and vomiting frequently followed and the drug was then administered rectally. On the second, third and subsequent days, adults were given daily from 3 to 4 Gm. in fractionated doses. The total dose, administered in the course of from five to seven days, varied between 15 and 25 Gm. Better results were obtained with these large doses than with the more prolonged administration of smaller doses. Children tolerate sulfapyridine well and can be given from one half to one tablet of 0.5 Gm. of the drug from two to four times daily. In addition to the sulfapyridine the patients were given cardiac and circulatory stimulants. The drug proved successful for patients of all ages and against the different types of pneumococci. Especially noteworthy is the favorable action on type III (mucosus), which does not respond to serotherapy. Even cases in which there was involvement of several lobes, with bacteremia, responded well. The treatment was the more effective the earlier the medicament was administered. Fifteen patients died, but five of these were already moribund when hospitalized and the treatment of six more was begun too late to be effective. Thus it may be said that only four of 293 patients died in spite of treatment with sulfapyridine. The author concludes that sulfapyridine is the method of choice in the treatment of acute lobar pneumonia.

Vestnik Khirurgii, Leningrad

58:479-622 (Dec.) 1939. Partial Index

Tetanus Prophylaxis. A. M. Zasludovskiy.—p. 485.

Complications of Serum Prophylaxis of Tetanus. E. V. Usoltseva.—p. 494.

*Procaine Hydrochloride Block in Acute Ileus. G. M. Novikov.—p. 506.
Procaine Hydrochloride Block Treatment of Carbuncles and Furuncles of Upper Lip and Corner of Mouth. S. A. Beylin.—p. 513.

Experimental Chronic Cystic Mastitis and Bleeding Breast. Ya. E. Sorin.—p. 517.

Significance of Mucous Plug in Injuries of Stomach and Bowel. S. S. Sharimyan.—p. 528.

*Undescended Testes: Operative Indications. A. Ya. Dukhanov.—p. 558.

Procaine Hydrochloride Block in Acute Ileus.—Between 1936 and 1938, 139 patients with acute intestinal obstruction were admitted to the surgical clinic of Novikov (Leningrad). Sixty-three of these were operated on, while seventy-six (55 per cent) got well on a conservative regimen whose main feature was the lumbar procaine hydrochloride block as practiced by Vishnevskiy. The patient is brought direct from the admitting room into the operating room. From 50 to 100 cc. of 0.25 per cent

procaine hydrochloride is injected into the right or the left renal fossa. In forty-six of the seventy-five cases the procaine hydrochloride block alone resulted in from thirty to sixty minutes in a diminution of pain, passage of flatus and a copious bowel movement. In twenty-nine the block relieved the pain and caused some passage of flatus but no stool. Siphoning enemas brought about passage of feces. Five patients were treated with enemas alone without result. Induction of the procaine hydrochloride block caused flatus and stool in from twenty to sixty minutes. Of twenty-two patients with obstruction due to postoperative adhesions, seventeen were relieved by the procaine hydrochloride block and three by the block supplemented by enemas. The *modus operandi* of the lumbar procaine hydrochloride block is probably to be seen in the removal of the irritating factor, result of anesthesia of a wide network of the vegetative nervous system. The method offers the possibility of preoperative recognition and of effective treatment of functional ileus. The method may likewise prevent the transition of a functional ileus into a mechanical one.

Undescended Testes.—Dukhanov reports on forty-four patients with undescended testes, thirty-three of whom were operated on and eleven of whom were treated conservatively. Follow-up was possible in twenty cases. Increase in the size of testes which were brought down was noted in only four cases. In twelve the testes were atrophied, in five of these almost completely. Orchidopexy per se apparently did not exert a stimulating influence on growth of the testis. The occurrence of complications of a retained testis is too rare to constitute an indication for operative intervention. Complaints of pain of continuous or spasmodic character on the part of the patient constitute, in the author's opinion, an absolute indication for intervention because it suggests a tendency on the part of the retained testis to strangulation or to torsion of the spermatic cord. Sixteen of twenty patients had complete relief from pain. The author's impression, based on his observations and review of the literature, is that the great majority of the ectopic testes descend spontaneously about the time of sexual maturity and considerably later. Such testes not infrequently develop and reach normal size. The favorable effect of treatment with gonadotropic substance on the descent and growth of the testes suggests that the pathogenesis of cryptorchidism is dysfunction of the endocrine apparatus.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

84:1285-1384 (April 6) 1940. Partial Index

- Thrombosis of Coronary Artery. L. P. Daniels.—p. 1286.
 *Changes at Mouth of Esophagus in Plummer-Vinson Syndrome (Dysphagia with Anemia). P. G. Gerlings.—p. 1289.
 Evacuation and Measles. H. I. de Ruiter.—p. 1297.
 Special Form of Leukemia. J. J. de Jong.—p. 1301.

Esophageal Changes in Dysphagia with Anemia.—According to Gerlings, the concurrence of hypochromic anemia with dysphagia, the so-called Plummer-Vinson syndrome, is often seen first by laryngologists, because dysphagia is generally the chief complaint. The majority of patients are middle-aged women who give a history of several years of dysphagia, the difficulty in swallowing being localized at the level of the larynx. They may have been taking only fluid and strained foods, because solid foods "get stuck in the throat." Examination often discloses a small mouth with rhagades at the corners and a pale oral mucous membrane. The lingual mucosa may be smooth as the result of atrophy of the papillae and, like the buccal mucosa, it may have patches of leukoplakia. There is dryness and perhaps atrophy of the pharyngeal mucosa. The anemia is of the hypochromic type. Koilonychia (spoon nails) is a frequent symptom. Achlorhydria is likewise frequent and in some cases the spleen can be felt. Internal therapy in the form of iron and hydrochloric acid improves not only the anemia but also the dysphagia. The author stresses the value of the x-ray examination and of esophagoscopy in patients with the Plummer-Vinson syndrome. They are essential in ascertaining the nature of the lesions at the mouth of the esophagus, such as stagnation of secretion in the pyriform sinus and just above the mouth of the esophagus, superficial ulceration and stenosis by scarring (in bands or in circular form). The possibility of carcinoma must always be kept in mind.

Acta Medica Scandinavica, Stockholm

104:1-233 (April 23) 1940. Partial Index

- *Further Observations on Zoster and Spinal Diseases. M. Kobro.—p. 1.
 Contribution to Question of Nervous and Muscular Substratum of Muscle Tone. Gösta Haggqvist.—p. 8.
 Microdetermination of Ester Sulfate in Blood and Pus. B. Norberg.—p. 21.
 Pernicious Anemia and Exophthalmic Goiter. T. Sténsliam.—p. 29.
 Clinical Observations on Course and Prognosis of Lymphogranulomatosis Benigna (Schaumann), Particularly in Regard to Pulmonary Lesions. T. Bruce and E. Wässén.—p. 63.
 Osteopoiikilosis with Dermatofibrosis Lenticularis Disseminata. M. Sjöholm.—p. 108.
 Cerebral Manifestations of Lymphogranulomatosis Benigna (Schaumann) and Uveoparotid Fever (Heerfordt). B. Roos.—p. 123.
 Schaumann's Disease (Benign Lymphogranulomatosis) with Erythrodemic Patches and Iridocyclitis as Dominant Clinical Symptoms. G. Nordin.—p. 131.
 *Effect of Prolactin on Secretion of Milk in Women in Puerperium and for First Few Months After Parturition as Well as in Newborn Babies. K. G. Kaijser.—p. 158.
 Hippuric Acid Test as Means for Determining Hepatic Function. A. J. Quick.—p. 216.

Zoster and Spinal Diseases.—Kobro observed six patients with vertebral lesions in whom zoster developed in segmental relation to these defects. One patient presented zoster scars in the third and fourth cervical segment, and x-ray examination disclosed ankylosis of the second and third cervical vertebrae. Another patient had destruction of the fifth thoracic vertebra due to myelomatosis, and zoster developed in the fifth thoracic segment. A third patient had Hodgkin's disease with involvement of the sixth thoracic vertebra, and zoster appeared in the sixth thoracic segment. Another patient had spondylolisthesis between the fourth and the fifth lumbar vertebra and zoster developed in the fourth lumbar segment. The objection may be made that the concurrence of zoster with vertebral lesions is a coincidence. However, each added case makes it seem more probable that a causal relation exists. The six cases of regional zoster with vertebral diseases have been found among a limited number. A methodical search was made for patients with vertebral lesions and zoster that was not in segmental relationship but none were found. Zoster in patients with vertebral lesions was always in segmental relation to the vertebral defects. It thus appears that a vertebral lesion may give rise to a regional zoster and, since vertebral lesions may exist for a time without symptoms, the appearance of zoster should direct attention to the possibility of a vertebral lesion. The fact that zoster is not a common but only an exceptional complication of vertebral lesions indicates that a ganglionic lesion alone cannot provoke zoster but that there must be another factor, and it is believed that this is the specific virus of zoster. The nonspecific lesion seems only to prepare the milieu for the specific virus of zoster.

Prolactin and Secretion of Milk.—Kaijser experimented with prolactin, the lactation-promoting hormone of the anterior lobe of the hypophysis. Prolactin is a hypothetical hormone which is not prepared in a chemically pure form but is obtained in an extract from the pituitary. The preparation used was an extract of sheep pituitary, free from demonstrable thyrotropic adrenotropic and gonadotropic factors. It was administered intramuscularly in quantities measured in daily pigeon doses. The author studied the amount of milk produced by 249 healthy women who did not receive prolactin. Studies on the effect of prolactin given during the first month after parturition revealed that no real increase in the supply of milk could be demonstrated except in cases in which prolactin was administered within a week of parturition. Prolactin was given also to women in whom hypogalactia appeared during a later stage of lactation. The results do not provide definite proof that prolactin has any real effect on the milk supply during the later stages of lactation. The author studied the effect of prolactin on the production of witch's milk in infants during the first few months of life. These babies have been under the same hormone influences as their mothers, and their mammary tissue may be imagined to have undergone similar preparation. Thus, if prolactin is of real value to lactation in the mother, its administration to babies during the first few months of life should provide some evidence as to its properties. In a number of cases the author succeeded in demonstrating a slight increase in the glandular tissue and in a few cases the appearance of milky fluid in small quantities on mild pressure on the breasts.

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THE PRESENT TREND OF TRANS- URETHRAL RESECTION

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Eight years has elapsed since Davis¹ first presented his paper on resection before the annual meeting of the American Medical Association in 1932. During this time a voluminous literature has been built up that has dealt with all phases of the subject. Enough time; it would seem, has elapsed so that a summary of the present status of resection is in order; if further justification were needed for the summary, the undeniable fact that a complete change of view has been effected during this time should give us pause.

During the early phase of the subject many articles dealt with the reasons why the procedure could not withstand the test of time and why it was not a sound one. Gradually an increasing number of articles dealing with the bad functional results were written, and attention was called to the number of complications.

As one might reasonably expect with any new and highly technical procedure, complications due to technical difficulties were reported, such as injuries to the urethra with rupture and urinary extravasation, perforation of the bladder with injury to the rectum, injury to the intestine with peritonitis, retroperitoneal cellulitis and intravesical explosions.

As the technic of the procedure was mastered, with the possible technical complications constantly kept in mind and every attempt made to avoid them, the number of these complications was greatly reduced.

During the past few years the number of patients who suffer from coronary thrombosis, attacks of angina pectoris, hypotension and hypertension has practically doubled, a fact emphasized in a previous publication.² Since that time there has been no change in this trend, and as a matter of fact many of these cardiac patients are sent in with the specific request that their obstruction be relieved by resection.

Many of these patients because of their cardiac condition are very poor risks for any major operative procedure. Transurethral resection, with its absence of shock and lower operative mortality and with fewer postoperative complications, is easily the method of choice in the management of these bad cardiac cases. The following case is an illustration:

History.—C. M., aged 78, admitted to the Presbyterian Hospital Aug. 22, 1938, had had attacks of angina pectoris for

twelve years. These attacks were characterized by severe precordial pain, with severe dyspnea. He stated that he had had at least 1,000 attacks of angina.

The prostatic symptoms began five years previously, and at this time he was advised not to have anything done because of the seriousness of his cardiac condition. His chief complaints were difficulty in starting the stream, terminal dribbling, incontinence, pain and burning on urination. The urinary symptoms gradually increased in severity, so that it was necessary for him to strain a good deal before starting the stream, and the straining frequently brought on an attack of angina pectoris.

Physical Examination.—He was well nourished and well developed. The head, neck and lungs were normal. Examination of the heart showed the borders slightly larger than normal, with no murmurs. The heart tones were faint, the rate and rhythm normal. The electrocardiogram showed myocardial damage. Rectal examination revealed benign enlargement of the prostate, grade 3 plus. There was 100 cc. of residual urine. Bilateral inguinal hernia was noted. The blood pressure was 166 systolic, 70 diastolic.

Laboratory Examination.—The urine contained no albumin, no sugar, no blood and no pus. The culture was sterile. The phenolsulfonphthalein test showed an output of 55 per cent in ninety minutes.

The blood count and blood chemistry were normal. The Kahn test was negative.

Operation.—A transurethral resection was carried out Aug. 23, 1938, under caudal anesthesia. Enough tissue was removed to pack tight a medicine glass. Microscopic examination showed benign hyperplasia of the prostate.

Postoperative Course.—After the resection the patient had a fever ranging from 100 to 101 F. for two days. The temperature was normal at the end of the second day. Convalescence was uneventful. The indwelling catheter was removed on the sixth postoperative day, and the patient was discharged on the ninth postoperative day.

With freedom from pain on urination and straining there has been marked reduction in both the number and the severity of his attacks of angina.

Examination Oct. 23, 1939, showed no residual urine.

Furthermore, the number of patients sent in for resection and the number who suffer from serious coexisting lesions also are on the increase. I refer to the patients who have had a resection of the rectum or colon for carcinoma, patients with metastatic carcinoma, patients with severe pulmonary lesions, such as marked emphysema, severe bronchitis and asthma, and patients with hemiplegia—a group of patients for whom the advantages of resection as against prostatectomy are of great importance.

Another definite trend at the present time is not to deny men in the older age group relief of their obstruction solely on the basis of their age. Because of the well recognized clinical fact that there is a very definite increase in operative mortality in each decade, men in the eighth and ninth decades were advised not to subject themselves to surgical prostatectomy.

With the advent of resection a definite trend away from this type of advice is obvious and men in these

Read before the Academy of Medicine, Toronto, March 5, 1940.

1. Davis, T. M.: Present Status of Prostate Obstruction, J. A. M. A. 99:1928 (Dec. 3) 1932.

2. Kretschmer, H. L.: Ann. Surg. 104:917 (Nov.) 1936.

age groups are advised to have a resection because of the lower mortality rate, so that one does not hesitate to relieve these patients irrespective of their age.

History.—J. D., aged 99, admitted to the Presbyterian Hospital March 26, 1938, had had urinary symptoms for four or five years. He complained of great frequency of urination, being obliged to void every thirty minutes during the day and every fifteen minutes during the night. There were severe dysuria, slowing of the stream and terminal dribbling. For the past eight months he was treated with testicular hormone, and as a result of this treatment his symptoms rapidly increased.

Physical Examination.—He was thin and poorly nourished and almost deaf. The head, neck and lungs were normal. The heart was enlarged to the left and the rate irregular; a loud systolic mitral murmur was heard at the apex. An electrocardiogram revealed an advanced coronary artery sclerosis. The blood pressure was 152 systolic, 70 diastolic. There was 60 cc. of residual urine.

Laboratory Examination.—Urinary albumin was reported 2 plus, blood 2 plus and pus 4 plus. Culture of the urine showed *Bacillus coli*. The phenolsulfonphthalein test showed an output of 75 per cent in ninety minutes. The Wassermann test was negative. The blood urea nitrogen was 28.4 mg. and nonprotein nitrogen 45 mg. Red blood cells numbered 3,600,000 and white blood cells 9,200, and the hemoglobin content was 72 per cent.

Röntgen Examination.—No stone appeared in the urinary tract. Intravenous pyelograms revealed a slightly dilated lower ureter on the right and a double pelvis on the left. A cystogram showed multiple diverticula.

Operations.—March 30, 1938, an electroresection of the prostate was carried out under caudal anesthesia. A half medicine glass of tissue was removed. The temperature returned to normal on the second postoperative day. Several examinations for residual urine revealed 60 cc. April 18 a second resection was performed, and enough tissue to fill three medicine glasses was removed. The microscopic diagnosis was benign hyperplasia of the prostate gland.

Postoperative Course.—After the second resection convalescence was smooth and uneventful. The catheter was removed on the second postoperative day, and on the seventh day the patient left the hospital.

Examination a year and a half later, when the patient was 101, was negative as there were no complaints on his part. Residual urine measured 10 cc.

Shortly after the inauguration of resection it was severely criticized because of some of the bad results which followed its use. The method was criticized without taking into consideration the man who sat at the other end of the resectoscope. The same criticisms might be made of any surgical procedure. Here, as in any other form of surgery, it must be recognized that criticism and evaluation of any new form of surgical treatment must take into consideration the surgeon who carries it out, his qualifications, training and aptitude, especially in a highly technical procedure such as resection.

For example, in one case the procedure was criticized because it failed to relieve the symptoms when as a matter of fact failure was due not to the method but to the fact that the operator removed only a small part of the obstruction and overlooked the presence of a large stone in the bladder. Removal of the stone and complete removal of the obstruction resulted in a cure.

History.—A. G., aged 53, admitted to the Presbyterian Hospital Sept. 12, 1939, had a transurethral resection performed elsewhere fourteen months before. He received no relief whatever from his symptoms. His complaints on admission were extreme frequency of urination both day and night so that he was obliged to void every half hour, slowing of the stream, terminal dribbling and great pain and burning during the act of micturition. He frequently noted blood in the urine.

Physical Examination.—He was emaciated and appeared to be ill. A number of furuncles were scattered over the body. The head, neck, heart, lungs, abdomen and external genitalia were normal. The blood pressure was 140 systolic, 90 diastolic. On rectal examination the prostate was twice the normal size. There were no signs of carcinoma.

The blood count and blood chemistry were normal. Urinalysis showed albumin 4 plus and pus. Culture of the urine yielded short chain streptococci and *B. coli*. A catheter passed easily into the bladder; a sensation of grating was obtained, which was interpreted as being due to the presence of stone in the bladder.

Röntgen Examination.—A bladder stone the size of a peach appeared. Intravenous pyelograms were normal. A cystogram showed numerous small diverticula.

Operation.—Sept. 13, 1939, a suprapubic cystotomy was performed and the stone removed. The bladder was drained for ten days, and September 25 a transurethral resection was done under sacral anesthesia. Examination with the resectoscope revealed large middle, intra-urethral and intravesical lateral lobes. Two medicine glasses of tissue were removed. Histologic examination revealed benign hyperplasia.

During the postoperative course acute pyelitis developed and on the thirteenth day there was a secondary hemorrhage. The clots were evacuated with a Bigelow pump and the bleeding points fulgurated. Two days later he was given a blood transfusion of 500 cc. He was discharged October 1.

Examination on October 24 showed no urinary symptoms and there was no residual urine.

Clearly the persistence of symptoms following the first resection cannot be charged to the method as such.

It is very interesting to note that although this method was taken up with avidity in this country, in Europe the urologists looked somewhat askance at the procedure and for long were doubtful of its beneficial effects. Bruni,³ in a recent publication, calls attention to this fact and asks "Could this have been due to faulty technic or imperfection of instruments?"

An interesting statement was made recently by Riba⁴ with regard to the major points in the discussion. He said: "Considerable credit should be given to those who are well trained in open surgery but who for the benefit of the patients have pursued the transurethral method and mastered its technic."

The historical review of this subject, the development of the various types of instruments used, the advantages of this method, the necessity for careful preoperative study and preparation of the patient, the dangers and complications, all these important matters have been more or less expatiated on by many authors at various times; hence a repetition here of what has been written on the subject would be superfluous.

Whereas formerly there was much difference of opinion regarding the type of patient who should have a resection there is one definite common ground on which all urologists agree: Practically all believe that the small bars, contractures, small middle lobes and small intra-urethral lobes are best handled by resection, and most urologists agree that the carcinomatous prostate when it produces obstruction should be handled by resection. It goes without saying that a resection in cancer of the prostate is much to be preferred to a permanent suprapubic fistula, even if a second and third resection become necessary. Moreover, many patients who are afflicted with carcinoma of the prostate are seen so late in the course of the disease that only a small percentage are amenable to radical surgery.

3. Bruni, C.: *J. belge d. urol.* 11: 78 (April) 1938.

4. Riba, L. W.: *Internat. Abst. Surg.* 68: 74-92, 1939, in *Surg., Gynec. & Obst.*, January 1939.

The only debatable point centers around the treatment of the large prostate. Here opinions still differ. On the one hand, the surgically minded have taken a definite stand that large prostates should be removed by open surgery, whereas many urologists believe that even very large prostates should be resected. This is a very debatable point since a prostate that has been diagnosed as being too large for resection by one physician, who says it must be removed by prostatectomy, is subsequently removed by resection by another. Another interesting fact is that as the experience of the operator increases, the number of his resections increases and the number of prostatectomies decreases, which is akin to stating that as one's experience increases the number of prostatectomies decreases because the proficiency of the operator permits him to resect the large prostates.

Whether or not resection will ever completely replace prostatectomy is open to question. In a previous publication I stated that in the fifty-one months prior to 1936 I had performed only one prostatectomy, all other patients having been treated by resection. Since this statement was made in 1936 I have performed one suprapubic prostatectomy and the reason I performed it was the fact that it was impossible to introduce the resectoscope. T. M. Davis is of the opinion that prostatectomies are mandatory in 2 per cent of the cases.

The question of whether or not the very large prostate should be treated by resection or prostatectomy may automatically solve itself, when in the future the patient with prostatism will seek relief early rather than late in the course of the disease, long before the prostate reaches an enormous size and prior to the onset of the severe distressing symptoms which occur late in the course of the disease.

Once he is aware of the fact that he may obtain relief by a method that has in its favor a low mortality rate, with a much shorter period of morbidity, with fewer and less serious complications and with good functional results, it is reasonable to assume that the prostatic patient of the future will seek relief early rather than late in the course of the disease.

Early relief of prostatic obstruction changes the clinical picture of obstruction as far as many of the associated pathologic conditions are concerned. The results of long-standing obstruction of the bladder neck are well known. At first they are mechanical, resulting in diverticula or diverticulosis, hydro-ureter and hydro-nephrosis; sooner or later infection is superimposed and cystitis, ureteritis, pyelonephritis and infected hydro-nephrosis result. If the obstruction continues, renal atrophy with impaired renal function occurs, and finally uremia and death of the patient. Stone formation in the bladder and upper tract may occur, either before or after infection is added to the results of urinary obstruction.

If patients are treated early, the entire clinical picture is changed because these complications will not occur. Here as in other fields of surgery, the undeniable importance of early relief of obstruction is written large. In view of the fact that the late effects of obstruction are well known and have been known from time immemorial, that they can be prevented, and that when present they increase the mortality rate, it is difficult to understand the advice so often given a patient that an early operation is not necessary but that by watchful waiting, followed by an operation, many points will be gained.

Whereas formerly indications and contraindications were rather rigid, during the past few years a good

many urologists have become more liberal in selecting cases for resection. This liberalization applies especially to the patient with impaired renal function. If after careful preliminary study and after instituting adequate drainage and treatment the blood chemistry studies show relatively high values, resection is carried out; it should be borne in mind that as a result of the long-standing obstruction, a certain amount of renal damage that is irreparable has taken place and because of this the function will never return to normal.

As one's experience with resections increases, resections are carried out in the presence of larger amounts of residual urine without preliminary catheter drainage, or with shorter periods of drainage. Thus at the present time resection is done without preliminary drainage in the presence of 6, 7 or even 8 ounces of residual urine provided the renal function is good, the urine grossly clear and the heart and lungs in good condition.

These remarks, however, are not to be misconstrued and to be interpreted to mean that one should dispense with careful preliminary study and preparation. What I attempted to state was that a good many urologists have liberalized their own personal indications and contraindications based on their personal experience.

When resection was introduced a good many preliminary cystostomies were done, and some urologists advised this as a routine before doing a resection. I have never subscribed to this procedure but have used preliminary drainage in the cases of very bad infection and in the presence of large or multiple stones. In other words, I weighed the pros and cons carefully with regard to the cases in which a preliminary cystostomy was indicated.

During the past few years the number of preliminary cystostomies indicated has become less and less. This may partly be explained because of increased experience, but the major reason is that the patients seek relief earlier (encouraged by the results of resection) and thereby reduce the number of bad infections.

In this connection it might be well to discuss a small group of patients who have marked urinary symptoms, whose prostates are small or normal in size on rectal examination and who have a small amount of residual urine. It is perhaps this group to whom the criticism is directed that many patients are being subjected to resection who should not be operated on at all. They might well be classified as on the borderline; hence at times it may be extremely difficult to make a decision. Under these circumstances, I institute a course of local treatment—namely, sitz baths or heat by rectum, massage, instillations and the internal use of sedatives such as hyoscyamus and bromides. If this regimen should fail to relieve the patient I advise a resection. In this group of patients the rectal examination may show the prostate normal or only slightly enlarged, whereas the instrumental examination shows the presence of well marked intra-urethral protrusion of the lateral lobes.

The present status of the treatment of diverticula associated with prostatic obstruction is a matter that should invite discussion. Whereas in the days of suprapubic and perineal prostatectomy all diverticula were removed, at the present time there is a very definite tendency not to remove them as a routine procedure. As a matter of fact, I no longer perform routine diverticulectomies.

In discussing the treatment of diverticula, it is necessary to assume that the obstruction at the bladder neck has been removed completely. It is well known

that if the obstruction has been completely removed, many diverticula tend to decrease in size and produce no subjective symptoms. The question as to whether the diverticulum or diverticula should be removed will depend on several factors and demands individualization.

1. *Small Diverticula*.—I do not remove small diverticula if the obstruction is removed completely, the urine is clear and subjective symptoms are absent.

2. *Larger Diverticula*.—Here again, if the obstruction has been completely removed, if the patient is free of symptoms, if the urine is clear or slightly hazy owing to bacteria and contains a few pus cells, and if the diverticulum is not close to the ureter so as to produce ureteral obstruction, I am of the opinion that administering urinary antiseptics and keeping the patient under close observation is all that is necessary.

However, if the ureter is obstructed, the pyuria does not clear up and there are recurring attacks of chills and fever, accompanied with urinary symptoms, or if the diverticulum does not empty, I believe the patient should have a diverticulectomy.

3. *The Very Large Diverticula*.—Here of course one must take into consideration the size and number of the diverticula, whether or not there are manifestations of peridiverticulitis, whether or not the diverticulum retains urine and hence is a source of infection, the amount of infection in the urine and the relation of the ureter to the diverticulum. As a rule, I remove the large diverticula first and then perform the resection.

During the early days of resection, most urologists were satisfied to remove just enough tissue to make a channel through the prostatic urethra. It soon became evident that this procedure was not sufficient and that a larger amount of tissue must be removed. Some, if not a good many, of the early patients who subsequently required a second resection undoubtedly belong to the group who had an insufficient amount of tissue removed. However, as one's experience with this method grows, more and more tissue is removed, and many urologists are of the opinion that the whole prostate should be removed. With this view I am in complete accord and I believe the term transurethral prostatectomy would be justified.

TABLE 1.—Amounts of Residual Urine in First Group of 273 Patients Tested After Transurethral Resection

Amount	Cases	
	Number	Per Cent
No residual.....	181	66.30
11-20 cc.....	41	10.11
Total 82.41 per cent		
21-30 cc.....	17	6.22
31-40 cc.....	5	1.83
41-50 cc.....	6	2.19
Over 50 cc.....	20	7.32

As has been previously mentioned the objective of the treatment of prostatic obstruction, whether by perineal or suprapubic or by transurethral resection, is to remove the obstruction completely, and if the obstruction has been completely removed a cure will result. Whether or not the obstruction has been completely removed can best be determined by demonstrating the presence or absence of residual urine. It seems to me that this is a very critical evaluation of the result obtained.

If one method is just as effective as the other in relieving the obstruction completely, if it carries with it a lower rate of morbidity and mortality, and if it can be used in patients who are "poor surgical risks," then it seems to me that that particular operative procedure should be the one of choice.

TABLE 2.—Amounts of Residual Urine in Second Group of 31 Patients Tested After Transurethral Resection

Amount	Cases	
	Number	Per Cent
No residual.....	207	73.52
11-20 cc.....	33	12.85
Total 87.00 per cent		
21-30 cc.....	10	6.95
31-40 cc.....	2	0.73
41-50 cc.....	2	0.73
Over 50 cc.....	10	3.71

It might be well to call attention to the fact that small amounts of residual urine present at the time the patient is discharged from the hospital gradually disappear. Even large amounts of urine tend to disappear completely, provided the obstruction has been completely removed. When large amounts of residual urine persist for more than a few weeks after resection and when repeated examinations show that the obstruction has been removed, one naturally becomes interested in determining the cause of the large residual. In this type of case one's attention is naturally turned toward the possibility of lesions of the central nervous system or to the possibility of muscular atony.¹

If the patient suffers from some lesion of the central nervous system that was recognized before the resection, the question naturally arises with regard to the possible role that it might play, and hence another neurologic study is in order. Atrophy of the bladder wall may be the responsible factor, although it is exceedingly rare; however, great care must be exercised to rule out mechanical obstruction as well as disease of the central nervous system before the final diagnosis of atony is made.

I would like to mention two patients whose obstructions were completely removed, and yet after they left the hospital they had large amounts of residual urine, 750 cc. in one case and 700 cc. in the other. Recent examinations show the complete absence of residual urine in both of these patients.

In a certain number of patients a coexisting pathologic feature is the cause of residual urine, such as one or more large diverticula or a large amount of hydronephrosis. Once in a while a patient may return a year or two after resection with residual urine and a recurrence of the characteristic symptoms. Examination will reveal a carcinoma of the prostatic bed.

HEMORRHAGE

During the early days of resection bleeding during the operation was very troublesome, and instances have been reported in which it became necessary to perform a suprapubic cystostomy in order to control the bleeding. This untoward occurrence led to much discussion. Here again, as in other technical phases of resections, increased experience and persistent search for the bleeding points so that they could be treated with the coagulating current ameliorated matters considerably. Today hemorrhage during the operation has ceased to be much of a problem.

A hemorrhage which occurs during the second post-operative week is probably always due to a secondary infection. Its treatment has become standardized and consists of evacuation of clots, if present, and visualization and fulguration of the bleeding point or points. At times it may be advisable to resect the bleeding area. If the bleeding cannot be controlled, a Foley bag may be used.

Suprapubic cystostomy is rarely if ever needed in this type of case.

In a previous publication I called attention to a type of bleeding that occurs one, two or even three years after resection. I wish to call attention to this type of bleeding because it has not received much consideration in the literature.

When late bleeding occurs one is naturally interested in the cause. It may be due to a stone in the bladder—that has formed since the resection, to a tumor of the bladder or to infection in a diverticulum. In some of my cases late bleeding was due to a tumor of the bladder which was resected and fulgurated at the time of the prostatic resection but which had recurred. In an occasional case late bleeding may be due to a renal tumor, nephrolithiasis or hydronephrosis.

In cases of resected carcinoma of the prostate late bleeding is always due to a recurrence of the growth.

If the causes just mentioned have been excluded, careful examination may show the presence of varices in the prostatic urethra and at the internal urethral orifice; however, in the larger number of cases careful examination shows the presence of more or less prostatic tissue, clearly indicating that not enough tissue was removed at the time of the first resection.

Finally, I have never seen late secondary bleeding in cases of small fibrous prostates or median bars.

VASECTOMY

It might be well to call attention to the present trend away from performing vasectomies.

During the early period of resection, vasectomy was recommended and used by a very large number of urologists as a routine procedure, the object of which was to prevent postresection epididymitis.

At the present time there is a decided trend away from vasectomy as a routine procedure.

TABLE 3.—Amounts of Residual Urine in 234 Recent Patients Tested After Transurethral Resection (Third Series)

Amount	Cases	
	Number	Per Cent
No residual.....	210	89.74
11-20 cc.....	16	6.83
Total 96.57 per cent		
21-30 cc.....	4	1.28
31-40 cc.....	1	0.42
41-50 cc.....	2	1.28
Over 50 cc.....	1	0.42

In my first cases vasectomy was not employed. In 12 per cent of this series there was postresection epididymitis. I then employed vasectomy as a routine for several years.

For the past three or four years I no longer perform vasectomy except under certain circumstances which I shall mention. In my recent experience postresection epididymitis is uncommon. I have reviewed 250 recent cases at random from my records at the Presbyterian

Hospital and found that epididymitis developed in only five of them, an incidence of 2 per cent. In rare instances epididymitis may develop two, three or four weeks after the patient has left the hospital, but this complication is exceedingly rare, and if the patient lives outside the city, he may fail to report it. Because of my experi-

TABLE 4.—Analysis of Cases with 25 Cc. or More of Residual Urine Following Transurethral Resection

Patient Age	Residual	Complications	Comment
E. B. 66	25 cc.	Bilateral hydronephrosis, bilateral hydro-ureter	Last check-up 6 months ago
R. E. 69	30 cc.	Urethral stricture, hydronephrosis, hydro-ureter	No urinary difficulty a few weeks ago
C. K. 71	30 cc.	Carcinoma of prostate, bladder diverticulum, prostatic calcull	Under treatment
B. S. 73	30 cc.	Bladder diverticulum, urethral stricture	
J. W. 68	35 cc.	Carcinoma of prostate, bladder diverticulum	Urine clear 6 months ago
J. J. 77	50 cc.	Strictures, prostatic stones, bilateral hydronephrosis, hydro-ureter	No symptoms
C. U. 75	50 cc.	Under treatment
I. W. 68	15 oz.	Hypotonic myogenic bladder	Patient died 7/16/39

ence I no longer feel that vasectomy, as a routine procedure, is indicated.

Vasectomy is employed for patients who come to the hospital with a severe acute attack of epididymitis and are in need of catheter drainage because of complete retention or a large amount of residual urine and with infected urine. This group is not large.

As has been previously mentioned, the object of the treatment of prostatic obstruction is the complete removal of the obstruction. Whether or not this has been accomplished can best be determined by an examination of the patient for the presence or absence of residual urine.

I wish to present data for three groups of patients who were examined for the presence or absence of residual urine following transurethral resection (tables 1, 2 and 3). Figures for the first two groups have been previously reported.⁵ They are presented again for purposes of comparison with the third, or recent, group.

A review of these three groups of patients reveals the interesting fact that there has been a very definite increase in the number who had no residual urine as well as in decrease in the number who had from 10 to 20 cc. In the first group there were 66.3 per cent with no residual, in the second group 75.8 per cent and in the third group 89.7 per cent. Likewise there was a definite decrease in the number who had from 10 to 20 cc., namely, 16.1 per cent, 12 per cent and 6.8 per cent respectively. These two groups made up 82.41 per cent in the first series, 87.9 per cent in the second series and 96.57 per cent in the present series.

Likewise there has been a definite reduction in the number of patients who had over 50 cc. of residual: 7.32 per cent, 3.76 per cent and 0.42 per cent.

In this series there was only one patient who had over 50 cc. of residual urine.

122 South Michigan Avenue.

THE PROPHYLAXIS OF PYELO-URETERITIS GRAVIDARUM

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Pregnancy complicated by infections of the upper portions of the urinary tract presents a problem which has baffled obstetricians for many years. Not only have the etiology and course of the disease process not been clearly understood, but its treatment and, more particularly, its prevention have been quite empirical and often lacking in effectiveness. During recent years, intensive work on the problem has clarified some of the factors concerned in the etiology, enabling us to establish means of prevention. In addition, therapeutics of the infection itself has undergone most revolutionary changes, so that now we may view the disease with justifiable equanimity. As some of the more recent modes of treatment are not widely used and because there will always be need for constant vigilance as well as training of physicians to prevent the occurrence of the disease, we present this report, which will outline the treatment in use at the New York Lying-in Hospital as well as give the results of our experience.

Effectiveness in carrying out the provisions of any system of antepartum care designed to reduce morbidity from urinary tract infections requires that some of the etiologic factors be fully appreciated. At the outset, therefore, it may be well to consider those factors that are most essential to our purpose, namely the reduction of the incidence of pyelo-ureteritis.

ETIOLOGY

For an inflammation to develop in the tissues of the kidney pelvis and the abdominal ureter, two conditions must necessarily be existent. The first of these is stasis of urinary flow and the second is the presence of an inflammation-producing agent which can develop in such an environment. Unfortunately for our child-bearing women, in over 80 per cent of them marked stasis develops in the right ureter and, to a lesser degree, in the left one also. We cannot go into all the causes which contribute to the development of this urinary stasis, but for practical purposes it will suffice if we mention two: first, hormonally produced atony of the musculature of the tract and, second, the occlusive effect of the pregnant uterus bearing on the ureters. Atony of the musculature, on the one hand, with the presence of an obstacle to be overcome, on the other, contribute to produce the condition which has come to be recognized as the "physiologic hydro-ureter and hydronephrosis of pregnancy." As stated, this prerequisite to inflammation exists in approximately 80 per cent of pregnant women. Thus pregnancy itself may truly be said to provide the background most suitable for inflammation of the urinary tract, which explains why pyelo-ureteritis is so much more frequently seen during the reproductive period of a woman's life than at any other time, with the possible exception of childhood.

The second prerequisite for infection of the upper urinary tract is an organism capable of living in the

environment of the ureter and of producing an inflammatory reaction in the tissues of the ureter and renal pelvis. The pathogenic agent which most frequently qualifies as a primary invader in these respects is some member of the large family of colon bacilli. The secondary invaders are most frequently anaerobic nonhemolytic streptococci, which are relatively non-pathogenic and produce inflammatory effects only in tissues previously injured by some other organism or by trauma. As the human body normally harbors huge numbers of colon organisms, it is not surprising that pregnancy with urinary stasis should be complicated by inflammatory reactions of the urinary tract due to the colon bacillus. How the organisms reach the upper urinary tract is a matter pertinent to our consideration of prophylaxis, so we may well point out that the two most salient factors, in all probability, are constipation of the large bowel and trauma of the lower portions of the urinary tract. Both of these are instrumental in allowing the coliform organisms to reach the upper urinary tract, where, if they arrive in sufficient numbers, they may cause inflammatory effects.

This brief and necessarily incomplete consideration will suffice to explain the causation of primary attacks having their incipience in pregnancy; however, the matter of etiology is unfortunately not quite as simple as this. We must also recognize the fact that previous attacks of pyelo-ureteritis may not have been completely cured and that many women carry a chronic type of afebrile and asymptomatic pyelo-ureteritis for years. This chronic type of infection may flare up as an acute exacerbation when the urinary stasis of pregnancy provides a locus of reduced resistance. An appreciation of the possible role of previous urinary tract inflammation is one of the most necessary points of view for the obstetrician to acquire, if he is to deter the incidence of urinary tract inflammation in the pregnant woman.

INCIDENCE OF PYELO-URETERITIS GRAVIDARUM

The appearance of inflammation of the upper urinary tract complicating pregnancy varies in its frequency and is dependent on many factors which are not wholly understood. For instance, Baird reports an incidence of 15 per cent in the Glasgow Royal Infirmary, whereas van Rooy reports only 0.8 per cent in Amsterdam. A common expectancy would probably vary from 1.5 to 2.5 per cent in communities where women of child-bearing age have average standards of living with adequate nourishment and good medical care.

PATHOLOGIC COMPLICATIONS OF INFLAMMATION OF UPPER URINARY TRACT IN PREGNANCY

Before presenting the means of avoiding the disease it is well to understand some of the more serious possibilities that we are attempting to obviate. One must consider these in two distinct categories, the immediate and the remote. The immediate hazards which pyelo-ureteritis presents are:

1. Anemia due to the hemolytic effect of the colon organisms on the red blood cells. Although this may not of itself constitute a grave menace, it is often a considerable handicap in treating the disease, which may require blood transfusions.

2. Bilateral involvement of the tracts, which is more serious. Bilateral disease always carries with it a more grave prognosis, which fact will become more evident as we discuss the next possibility.

3. The most serious complication of all, namely ascension of the inflammatory process from the excretory ducts into the

renal cortex. Whenever this occurs, the obstetrician is confronted by a very serious problem, for not only is the excretion of urine impaired, with the retention of the nitrogenous products of metabolism within the blood stream and tissues of the body, but there is also danger of the patient's dying.

4. The immediate effects of acute pyelo-ureteritis on the fetus, which are of importance also, for premature delivery, stillbirth and even death a few days after delivery are not infrequently seen.

The remote effects on the mother are chiefly due to the fibrosis which the inflammatory reaction induces. This may permanently impair or prevent all peristalsis of the renal pelvis and ureter, resulting in constant hydronephrosis and hydro-ureter of the duct and in reduced secretory activity of the kidney cortex. In addition we must point out that, the longer the acute febrile phase is permitted to exist, the longer will be the period of time necessary to wipe out the infection after the pregnancy is over. Many experiences have impressed us with the truth of this statement, and in addition the literature on urinary tract complications of pregnancy is replete with confirmatory illustrations.

METHODS OF AVOIDING AND MINIMIZING THE DISEASE

With this brief outline of the disease in mind, we may turn to a consideration of the means whereby it may be altered for the benefit of the patient.

The first step which must be taken, and one which cannot be sufficiently stressed, is to obtain the history. Patients must be quizzed by name and symptom to establish or preclude the possibility that previous disease has involved the urinary tract. Over 50 per cent will give no definite history of pyelo-ureteritis at the time the anamnesis is recorded, and then later the patient's mother or aunt will reveal that there was such an event, particularly if an acute exacerbation occurs to remind them of the clinical picture. Emphasis is laid on the importance of the history because the chances that the disease will complicate pregnancy are increased twofold in previous sufferers and therefore one should be particularly observant of this group; but the history is emphasized more especially because the prognosis, should the disease reappear, is more discouraging than that pertaining to the primary acute attack. Not only is the infection more difficult, but in addition the scar tissue in the excretory ducts and the probability of decreased renal function must be taken into account if the best interests of the patient are to be served by her medical advisers.

The history having been taken, the obstetric patients divide themselves into two categories from a urologic point of view: those who have had previous attacks of pyelo-ureteritis and those who have not. First let us consider the antepartum care of the larger group, those who afford no history of previous inflammation of the upper urinary tract.

THE UROLOGIC CARE OF NORMAL OBSTETRIC PATIENTS

At each antepartum visit, the normal obstetric patient should be questioned concerning dysuria, frequency and pain in the kidney region. Should any of these be experienced, a sterile catheter specimen of bladder urine should be obtained and scrutinized microscopically. Should clumped white blood cells be seen, the remainder of the sterile specimen should be sent to the bacteriologic laboratory for culture. In the meantime, fluids are forced and the patient is given 4 Gm. of

sodium bicarbonate after each meal. If the culture is positive for *Bacillus coli*, the patient should be given the ambulatory treatment for urinary tract infection, which will be outlined presently.

Not infrequently the first indication of urinary tract infection is a cloudy precipitate produced in the urine by the test for albuminuria. When this is seen, in the absence of any supportive evidence for the diagnosis of toxemia, a sterile catheterized specimen of bladder urine should be taken and cultured for *B. coli*, whether any white blood cells are seen in the microscopic specimen or not.

Emphasis is placed on bacilluria as demonstrated by bacteriologic culture of the urine. This should be the basis of prophylaxis and not symptoms or the presence of pus cells in the urine.

As soon as the positive report of bacteriologic culture for *B. coli* is obtained, the patient is placed on what we have named our ambulatory sulfanilamide treatment. The patient is provided with twenty-five 5 grain (0.3 Gm.) tablets of sulfanilamide and is instructed to take one tablet on awakening, one after each meal and a fifth on retiring. With each of the postprandial pills the patient is instructed to take a teaspoonful of sodium bicarbonate dissolved in water. Fluids are limited to the lowest amount consistent with comfort (about 1,500 cc. daily). Of all the patients treated in this way, numbering about 200, only two have shown idiosyncrasy to the drug. With these small doses, the concentration of sulfanilamide in the blood rarely goes above 2 mg. per hundred cubic centimeters. Not only would this concentration seem devoid of danger, but many will wonder that it can be efficacious in a curative way. We shall offer statistics which prove beyond a doubt that the treatment is valuable in controlling the early stages of the infection.

The patient then returns for a repeat urine culture in a week's time. Even though the culture is negative, the course just described is repeated after one week's rest until a series of three negative urine cultures are obtained. Thereafter the urine is cultured once a month until delivery. Should a positive culture again be obtained, the ambulatory sulfanilamide therapy is repeated.

In brief, this constitutes the treatment of incipient cases. However if, as occasionally happens, the ambulatory treatment does not prove effective so that symptoms of pyelo-ureteritis such as pain in the costovertebral angle or persistence of pyuria occur, the patient is examined by cystoscope, the ureters are catheterized and bilateral ureteral cultures and pyelograms are taken. In this way the presence of inflammatory strictures of the ureter, hydronephrosis and hydro-ureter greater than those which occur physiologically are recognized, and appropriate treatment is instituted.

UROLOGIC CARE OF OBSTETRIC PATIENTS WHO HAVE HAD PREVIOUS INFECTIONS OF THE UPPER URINARY TRACT

The patient who offers a history of previous infection of the urinary tract is treated quite differently in that she is given less leeway because of the greatly increased chance of the development of infection during pregnancy.

If possible, contact is made with the hospital or physician who treated the previous infection, with a view to obtaining data concerning its severity and duration as well as whether the process was unilateral or

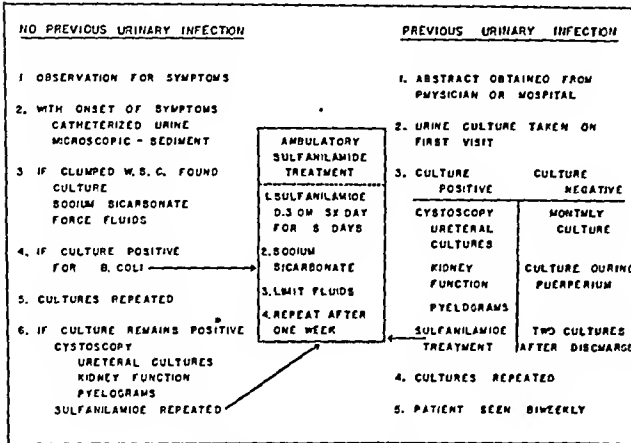
bilateral and whether kidney function tests were done, or whether there was evidence of damage to the renal cortex.

A culture of catheterized bladder urine is made on the first antepartum visit. If this culture is negative and the patient has no symptoms of pyelo-ureteritis, she is placed on routine antepartum care with the

partum antipyelitis regimen of forced fluids, frequent rest in the horizontal position during the day, with careful attention to adequate bowel elimination, and a broad general diet may suffice to carry the cooperative patient through to term, delivery and the puerperium without an acute attack. The postpartum care of all patients as a single group will be treated presently.

THE ACUTE ATTACK

Whether the acute attack occurs as a primary entity or as a recrudescence of long-standing disease, certain elements of therapy are fundamental. The first is hospitalization. Here bed rest in the completely recumbent position or with the foot of the bed elevated is given. Bladder cultures are repeated together with microscopic examination of the urine, to determine the type and severity of the inflammatory reaction. The blood nonprotein nitrogen level is determined every second or third day to rule out nitrogenous retention due to cortical damage. Intravenous pyelograms are taken to throw the kidney pelvis and ureters into view and also to give information as to kidney function. In addition, these patients are given large doses of sulfanilamide commencing with from 6 to 8 Gm. a day in divided dosages, with limited fluid intake the first two days, and thereafter a dose of the drug sufficient to maintain a concentration in the blood of from 8 to 10 mg. per hundred cubic centimeters and concentration



Urologic care of obstetric patients.

addition that urine cultures are repeated at monthly intervals until term; one is made in the puerperium and two after discharge from the hospital.

If, on the other hand, the initial urine culture is reported as positive for *B. coli* or anaerobic non-hemolytic streptococci, this together with the history of previous infection establishes the diagnosis of chronic inactive urinary tract infection and places the patient in a group which will receive very special attention and consideration, for in our experience over 40 per cent of them will develop an acute exacerbation before pregnancy has reached term if they are not given preventive care. A majority of these patients are examined by cystoscope and given bilateral renal function tests, while pyelograms are usually made at the same visit to determine gross abnormalities in the tract. Such a

TABLE 1.—Treatment of Acute Attack of Pyelo-Ureteritis

1. Hospitalization
2. Complete bed rest
3. Microscopic examination of urine
4. Bladder culture
5. Blood chemistry every two days
6. Intravenous pyelograms
7. Large doses of sulfanilamide

TABLE 2.—Treatment of Patient in Puerperium

1. Careful follow-up until three successive negative cultures are obtained at intervals of one month
2. Contraception for two years
3. Cystoscopy to rule out strictures
4. Repeated courses of sulfanilamide

patient is given the ambulatory sulfanilamide treatment in addition. If the tract shows no serious abnormality except the positive urine culture, she is followed at bi-weekly intervals to observe evidences of the early stages of the acute phase. In addition she is warned that, if kidney pain should supervene or if there should be chills and fever, she is to come to the hospital at once. On the other hand, if such an eventuality does not occur, it is entirely possible that the ordinary ante-

TABLE 3.—Results of Prophylactic Routine

	Before Sept. 1937	After Sept. 1937
Incidence of suspected cases of pyelo-ureteritis..	2.02%	1.00%
Incidence of proved cases of pyelo-ureteritis.....	0.80%	0.47%
Average duration of febrile phase.....	10.4 days	5.4 days
Average time after onset to obtain negative cultures	135 days	50 days
Negative cultures obtained during pregnancy....	0	33%

tration in urine above 100 mg. per hundred cubic centimeters. With the great majority of patients the temperature returns to normal after a few days of this treatment, and after three or four days of normal temperature the patient is discharged to be followed in the antepartum clinic.

Much to our surprise, about 25 per cent of the patients undergoing a primary acute attack who are admitted early in the febrile phase not only undergo remission but are also cured of their bacilluria. This is a distinct advance over older forms of therapy, experience with which yielded a widely accepted dictum to the effect that no patient was ever rendered bacteria free during pregnancy.

If, on the other hand, both ureters are involved and if the patient stores nitrogen as the result of persistent renal damage, interruption of the pregnancy has to be considered, just as in the older forms of treatment. However, in our experience, if there is careful observation so that the acute phase comes to treatment early and particularly if the acute phase is treated vigorously from the first, these more serious eventualities will seldom be met. In the past eighteen months we have been forced to induce labor prematurely on only one occasion, in marked contrast to our earlier experience.

TREATMENT OF THE PATIENT IN THE PUERPERIUM

The criterion of cure is three successive negative urine cultures taken at intervals of one month. This routine demands careful follow-up of the patient. In

In addition, further pregnancy is interdicted for a period of two years and the patient is given contraceptive advice and instruction in a technic suited to her needs.

Patients who have persistently positive urine cultures are given cystoscopic examination, and the possibility of ureteral strictures is ruled out. In addition, they are given repeated courses of sulfanilamide treatment until the desired negative urine cultures are obtained. In our experience, the longer the acute phase has existed the more difficult these final procedures become. We have had a few patients who have resisted all attempts to sterilize the urine for many months, and one for three years, which indicates clearly the importance of early recognition of the prodromal symptoms and prompt alleviation of the early forms of the acute attack.

RESULTS OF THE PROPHYLACTIC ROUTINE

Before September 1937, at which time this plan of care was instituted, the incidence of pyelo-ureteritis complicating pregnancy was 2.02 per cent including those having a majority of the symptoms of the disease and 0.80 per cent including only those who presented the well developed syndrome satisfying all criteria. Since September 1937 the incidence in the two groups has dropped to 1.06 per cent for clinically suspected cases and 0.47 per cent in the unquestionable group. In other words, the incidence of the disease has been reduced 50 per cent.

Just as important as the reduction of the incidence is a similar reduction in the duration of the febrile phase from 10.4 days, which was the average formerly, to 5.4 days, which is the record during the past eighteen months. This has a dual significance in that the briefer the febrile phase, the sooner the patient may be rendered bacteria free, thereby effecting an economic saving and enhancing the welfare of the patient.

Formerly it required an average of 135 days from the date of the acute attack to secure bacteria-free urine; now the average is fifty days after the onset of the disease.

As stated before, we now are able occasionally to sterilize the urine during pregnancy, that is, in about 55 per cent of cases, whereas formerly this was almost never possible. However, there are always a few patients who are disappointing, and our experience is no exception. We have two patients who have been treated most carefully and who have had repeated courses of sulfanilamide as well as cystoscopic treatment and who, despite our best efforts, continue to put out large numbers of coliform bacilli in the urine after many months of treatment.

Postpartum pyelitis has been almost completely eliminated by the use of small doses of sulfanilamide and sodium bicarbonate administered prophylactically to all patients having infected bladder urine with symptomatic cystitis.

In addition, pyclo-nephritis has come to be almost nonexistent because we do not allow the disease to progress to the point where this complication is possible.

SUMMARY

1. An antepartum routine designed to detect the earliest stages of upper urinary tract infection has been successful in pointing out patients who have primary attacks as compared with those having repeated exacerbations.

2. In the former group, small doses of sulfanilamide given with sodium bicarbonate have been useful in

obviating the disease in the prodromal phases. The incidence of febrile disease has been reduced 50 per cent.

3. Early availability of hospital care with vigorous treatment has succeeded in reducing the febrile phase by 66 per cent, as well as the length of stay in the hospital and the length of time necessary to render the urine sterile in the puerperium.

4. The more severe complications of the disease in the mother and child seem to have been largely obviated.

A BASIC UNDERSTANDING OF VARICOSE VEINS

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This article is being presented primarily for the benefit of the general practitioner in an attempt to clarify any confusion that may exist concerning the tests used in the examination of patients who have varicose veins. Any one who has perused the recent literature concerning varicose veins will verify the statement that the varied labeling of

the classic Trendelenburg test is confusing and frequently contradictory. In one of the most widely read surgical publications, articles of two well known writers in this field appeared a year apart in which were stated absolutely opposite meanings of a "negative Trendelenburg." The simple test has been expanded to include such modifications as "positive," "double positive," "negative" and "nil." Add to this, as examples, Perthes' test, the tight bandage test, the comparative tourniquet tests and the Schwartz test. Is confusion not to be expected from such

a situation? The practicing physician desires only to know what is wrong and how to correct it. So we will purposely not elaborate on or attempt to reexplain these obviously confusing nomenclatures. Literature has amplified them to the extreme. Our interest is to find out what is wrong anatomically and physiologically. That and the classification of observations under respective headings are primary. Rational therapeutics will then follow as a matter of course.

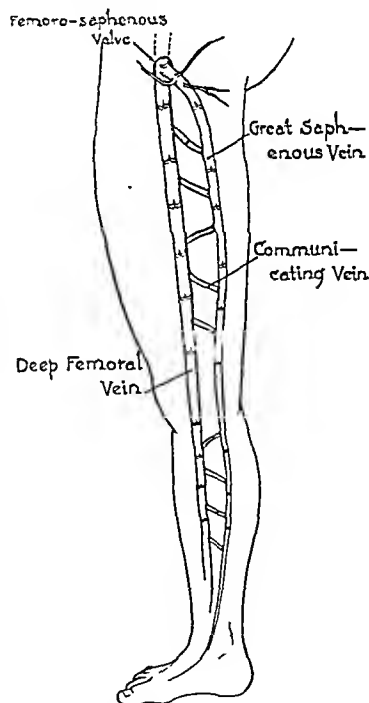


Fig. 1.—A simple diagrammatic scheme of the venous return from the lower extremity. The lesser saphenous vein has purposely been omitted.

The pathologic physiology of an incompetent saphenous vein was described by Trendelenburg¹ in 1890. He graphically demonstrated the reversal of blood flow and attributed this condition to disruption of valves at the saphenofemoral junction. On this basis he devised the simple yet adequate test for a definitely incompetent

normal anatomy and are represented in diagrammatic form in figure 1.

When visible and palpable varicosities are present there are three venous systems, anatomically, which may be affected: the superficial, the communicating and the deep (fig. 2).

INCOMPETENT GREATER SAPHENOUS (SUPERFICIAL) SYSTEM

The greater saphenous system should be the first to be investigated. The patient stands upright before the examiner with both legs fully exposed from the groin downward. The degree of dilatation and the distribution of the tortuous veins, the presence or absence of edema and cutaneous changes are noted. Palpation is of more value than inspection, for often large tortuous veins, not noticeable to the eye, can be felt in the subcutaneous tissues. To demonstrate incompetence of the venous system, the following method is probably the most practical: The fingers of one hand are placed over the great saphenous vein, usually at the fossa ovalis, while the fingers of the other hand percuss a dilated segment of vein in the leg below. The percussion stroke is an abrupt thrusting one so as to give rise to an impulse, much after the manner in which free fluid in an abdomen is detected by means of percussion. If the fingers at the fossa pick up a definite and strong impulse, incompetent valves and a dilated main saphenous trunk are strongly to be suspected. Proof, however, is established by a reversal of the procedure. If percussion of the vein at the fossa or in the upper por-

Fig. 2.—Incompetence of the three anatomic systems: *A*, inadequate superficial saphenous system; *B*, an incompetent communicating system (associated with failure of the superficial saphenous system); *C*, obstructing thrombosis of the deep system; compensatory dilatation of the superficial veins is necessary for adequate venous return.

greater saphenous system, a test which today bears his name. Yet forty-four years before Trendelenburg's paper Sir Benjamin Brodie² had described exactly the same method for determining the status of the superficial venous return from the legs. So we are detracting nothing from the credit of Trendelenburg when we urge physicians to discard the practice of employing a man's name to designate these tests and to speak rather in terms of what these tests indicate. In that way we shall train ourselves to visualize more perfectly the significance of each test, what is wrong and what is the rational method of treatment.

Venous return from a lower extremity is accomplished through two superficial saphenous systems and through a deep system. The superficial and deep routes are connected with one another by numerous communicating veins. These channels are necessarily equipped with valves to aid in the ascent of the venous blood and to prevent retrograde flow. Probably the most important valve is situated at or in close proximity to the saphenofemoral junction. Its impairment leads to gross incompetence of the greater saphenous vein. These are the simple relevant facts of

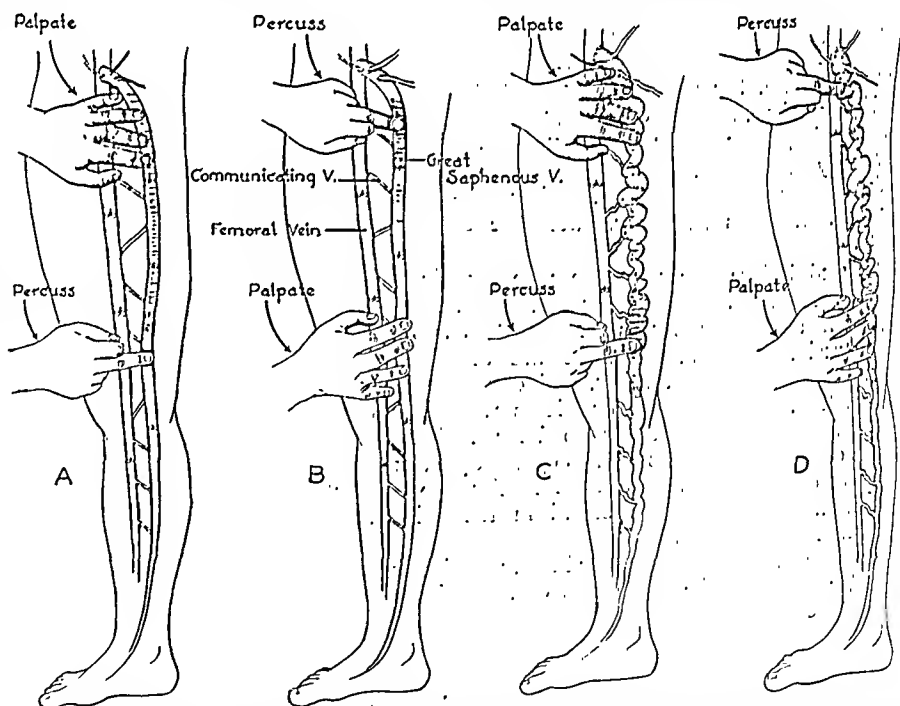


Fig. 3.—Testing for an incompetent greater saphenous system: *A* and *B*, a normal competent vein; intact valves prevent downward passage of the impulse; *C* and *D*, procedure used in detecting incompetent veins in which the valves do not impede the free passage of a strong impulse in both directions.

tion of the thigh produces an impulse which travels downward to the fingers below, and can be definitely felt, we know that the valves are incompetent and that the vein does not, and never will, perform its normal function. For such an impulse cannot travel distally in the vein if the valves are competent (fig. 3).

Owing to mechanical difficulties, such as marked obesity of the patient or extreme tortuosity of the

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2. Brodie, B. C.: Lectures Illustrative of Various Subjects in Pathology and Surgery, London, Longman (and others), 1846, vol. 7, pp. 157-191.

arices, only faint descending impulses may be discerned in some instances. The type of treatment then depends on the judgment of the examiner and his estimate of the amount of varicosities and the degree of vascular stasis present.

Examination of the superficial veins is never complete without a thorough investigation of the lesser

saphenous system, which drains the posterior and lateral aspects of the leg. Pathologic changes in the lesser saphenous system may be identical with those found in the greater saphenous system and the diagnosis can be made in the same manner. Treatment also is comparable and will be outlined. Various segments of the varicose trunks can be explored in like manner, and whenever we find a strong, definite, distalward impulse, we know that no adequate valve intervenes.

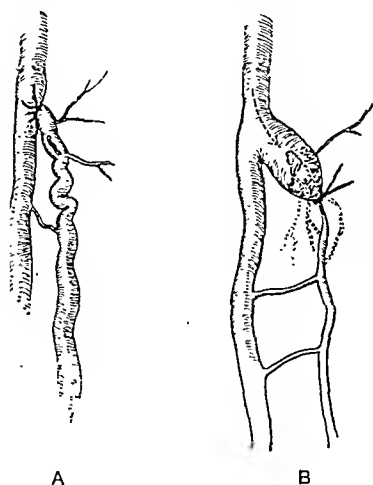


Fig. 4.—Ligation: A, correct site of ligation at the saphenofemoral junction; B, incorrect ligation, which leaves a blind stump to encourage the formation of new varicosities and to provide a site for the formation of a free thrombus (a ready source for multiple pulmonary emboli).

Although it is not necessary, we can confirm our deductions on the definitely incompetent greater saphenous veins by use of a tourniquet applied on the highest accessible portion of the thigh with the leg elevated and the veins drained of their blood. If, on standing, the veins fill rapidly from above downward after release of the tourniquet, we know that the valves do not hold; the vein is incompetent. In a similar way the lesser saphenous vein can be tested with a tourniquet applied just below the level of the popliteal space.

In conclusion, one should record whether the superficial saphenous systems are competent or incompetent and not that a certain test is "positive" or "negative." One can qualify the statement, if one wishes, by stating "as tested by palpation and percussion of the veins or by using a tourniquet." Use of the words "positive" and "negative" is likely to cause confusion when applied to any test, first because these terms are ambiguous and second because, if such terms are applicable at all, it is the result of a test and not the test itself that has "positive" or "negative" significance.

Brief mention should be made of the rational therapy for incompetence of the superficial saphenous systems pertinent to the pathology and physiology involved. Downward pressure of the column of blood in the inferior vena cava, common iliac, femoral and greater saphenous veins, unsupported by adequate valves, encourages further dilatation and elongation of the already varicose distal segments and provokes the gradual development of varices in previously unaffected veins. Local injections of sclerosing fluids alone for the obliteration of visible varices are likely to be followed by recurrences, particularly if the region treated is subjected to direct pressure from above. Such treatment is like clipping off the tops of weeds in the hope that they will not grow again. The roots must be destroyed in order to obtain such a result. So it is with

the reversed flow of blood in the incompetent greater saphenous system. It must be interrupted first at the saphenofemoral junction and then obliterated from that point distalward.

Cumulative experience has stressed the importance of high ligation of the incompetent greater saphenous vein in the prevention of recurrences. The ligation should be made at the fossa ovalis, exactly at the junction of the saphenous and femoral veins, without leaving any stump to encourage the formation of future varicose channels or to allow a free thrombus to form. Division of the vein between the two sites of ligation should be performed and a segment of vein should be excised at this site. All tributary veins joining the saphenous vein in this region also should be ligated and severed. This definitely lessens the probability of future recanalization (fig. 4).

Following ligation, retrograde injection of a sclerosing fluid (from 2 to 4 cc. of 5 per cent sodium morrhuate solution), as indicated, into the distal segment of vein is recommended as a valuable adjunct. The patient is allowed to be ambulatory immediately after operation and is not hospitalized further. Subsequent obliteration of the remaining varicosities is accomplished by repeated injections usually from above downward. If adequate ligation is not performed on an incompetent greater saphenous vein, recurrences are to be predicted. Of course, there are many cases of mild or moderate varicosities in which the saphenous systems are not incompetent. In such cases injection therapy alone suffices.

INCOMPETENT COMMUNICATING VEINS

Incompetent communicating veins are relatively uncommon, although much has been written concerning them. They are almost always associated with an incompetent greater saphenous vein, and clinical detection is easy. After the leg is elevated in order to allow the veins to be drained of their blood by gravity, a tourniquet is placed high on the thigh. The patient is then allowed to stand upright with the tourniquet still applied; if the varicosities fill rapidly within thirty sec-

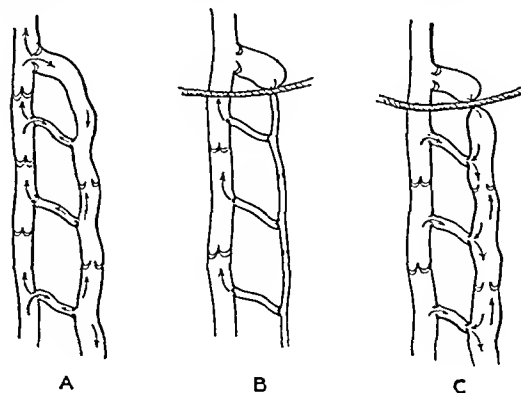


Fig. 5.—A, incompetent superficial and communicating systems; B, competent communicating system with tourniquet preventing reversal of flow in the incompetent superficial system; C, incompetent, communicating and superficial systems; an overflow from the deep to the superficial circulation through incompetent communicating veins with rapid dilatation of the superficial veins when the leg is lowered.

onds, it is assumed that there has been an overflow from the deep to the superficial circulation. In other words, the valves of the communicating vein or veins are incompetent. To eliminate error one must apply the tourniquet only tightly enough to obstruct the superficial veins (fig. 5).

Again for the sake of emphasis, let us stress the importance of stating the status of a system in terms

of competence or incompetence, thereby avoiding the expression "positive test" or "negative test."

Since incompetent communicating veins are usually associated with incompetence of the greater saphenous system, and since treatment for incompetent communicating veins involves, first, treatment for incompetence of the greater saphenous system, detection of the presence of incompetent communicating veins is not particularly vital. We believe that the injection of sclerosing fluids into the distal segment at the time of high ligation and subsequent injection of such fluids into the remaining varices will prevent retrograde flow through the communicating veins. This method, too, might be a subject for discussion and may have its uncertainties and occasional failures, but from a practical and financial standpoint it is preferable to extensive operative ligation of each communicating stem. If a recurrence follows at the site of the incompetent communicating vein, one may limit the segment of vein affected by the sclerosing fluid by injecting the vein between two tourniquets. The results are usually excellent with the formation of a firm thrombus in the offending segment adjacent to the incompetent communicating vein.

INCOMPETENT DEEP VENOUS SYSTEM

Persistent occlusion of the deep veins is a comparatively rare phenomenon, but it does occur. It is usually associated with marked edema and cutaneous

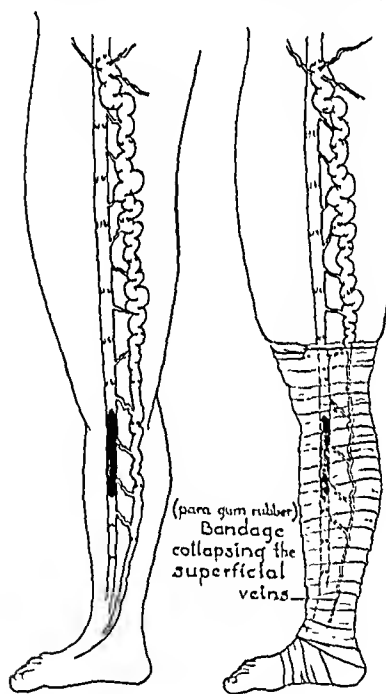


Fig. 6.—The only conclusive test for demonstrating an obstruction in the deep venous circulation. When such a condition is present, severe pain soon results from the blockage of venous return.

in place and to note whether with this activity his discomfort is increased or diminished. If the flow through the superficial venous system is a compensatory one, the constriction caused by the bandage will result in acute severe discomfort, because those veins which have assumed the function of allowing a return flow of blood from the extremity are compressed. Usually the patient returns within ten minutes with the bandage in his

changes. If edema is absent, one can almost exclude per se the possibility of complete blockage in the deep venous system. Usually there is a definite history of phlebitis with fever, soreness and swelling of the leg. Therefore, if it is suspected that such a condition exists, it is inexcusable for a physician not to determine its presence by applying a conclusive and simple test (fig. 6). A Para gum rubber bandage is applied around the leg usually from the instep to just below the knee or as far up the thigh as indicated. The patient is then instructed to walk about with this

hand and with an indignant expression on his face. Whereas, if the flow in the superficial veins is not compensatory and if a block is not present in the deep circulation, the bandage usually will give relief by collapsing the useless superficial varicosities.

The Perthes test is used in a routine manner by many to determine the status of the deep venous circulation. In the majority of instances it probably gives the

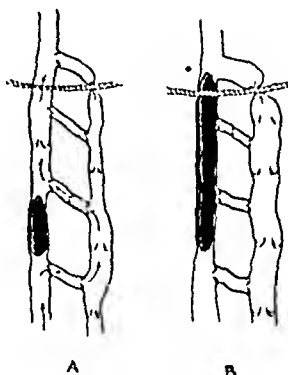


Fig. 7.—A, detour of venous flow around an obstructing thrombus in deep femoral vein; under such conditions the results of the Perthes test would be erroneously interpreted as normal; B, thrombus in deep circulation extends up to site of tourniquet; it is only in such a condition that the Perthes test can be correctly interpreted.

information desired, and yet many do not realize that there is an inherent flaw in the test. If a segment of deep vein is obstructed a thrombus anywhere below the upper level of the tourniquet, it is anatomical possible for a portion of the superficial circulation to detour around the thrombosed deeper vein and return to this vein proximal to the obstructed site. The tourniquet occludes the superficial veins only at one point high in the thigh and will therefore not obstruct the lower portion, which serves in the shunting mechanism. As this may easily occur, an incorrect interpretation results. The physician may

then block unknowingly with sclerosing fluids the superficial detour, and venous return from the lower extremity will be hindered even more than it was prior to such treatment. Therefore the test is inadequate, for this one flaw makes it unreliable (fig. 7). The bandage test is by far the better, for it definitely answers the question of whether the deep veins are patent or occluded. Obliterative therapy of any type, when definite deep venous occlusion is present, is absolutely contraindicated. Rest, elevation of the affected extremity, the application of heat and proper external support are the measures to be relied on.

SUMMARY

Acquaintance with the simple anatomy and physiology of the venous system of the lower extremities tends to clarify the confusion which exists with regard to test procedures and types of treatment for varicose veins. We urge abandonment of specific names for the various tests and acceptance of universal terms based anatomically on the three venous systems to be treated; that is, a test for competence or incompetence of the superficial saphenous system, a test for competence or incompetence of the communicating veins and a test for patency or occlusion of the deep venous system.

Renal Glycosuria.—In a small proportion of subjects glycosuria is due to apparently abnormal renal permeability. There are no precise figures concerning the incidence of this disorder, but it probably occurs about once out of every 300 to 500 cases of glycosuria. Renal glycosuria is a benign condition and is related to a low renal threshold. It is therefore distinguished from diabetes mellitus by the fact that the glycosuria is not accompanied by hyperglycemia; indeed the opposite condition of hypoglycemia may prevail.—Bodansky, Meyer, and Bodansky, Oscar: *Biochemistry of Disease*, New York, Macmillan Company, 1940.

THE DISTURBANCE OF CARBOHYDRATE METABOLISM IN HYPERTHYROIDISM

NATURE AND MANAGEMENT

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A significant and in some instances severe disturbance of carbohydrate metabolism has long been recognized in many patients with hyperthyroidism. Glycosuria, postprandial hyperglycemia and impaired dextrose tolerance occur in these patients and suggest the presence of diabetes mellitus. According to published data, the incidence of the first two factors varies greatly. However, the more or less uniform results of the dextrose tolerance test obtained by different investigators show that reduced tolerance to sugar is found in about one half of the patients with hyperthyroidism. A low respiratory quotient in the fasting state and a tendency to acidosis increase the resemblance of these symptoms of hyperthyroidism to diabetes. Finally, the aggravation of diabetes when hyperthyroidism is superimposed on it also points in this direction.

On the other hand, according to several metabolic criteria, the capacity of the tissues to utilize sugar is reduced in diabetes, while in hyperthyroidism it is increased. After the administration of dextrose in diabetes, the arteriovenous blood sugar difference is less than normal. This observation indicates that less sugar is taken up by the muscles. After a carbohydrate meal, the rise in the respiratory quotient is insignificant. When the supply of carbohydrates in the body is increased, the fall in the organic phosphates of the blood is less than normal. This fall is caused by the formation of a hexose-phosphate compound in the process of utilization of dextrose by the tissues. In contrast, after administration of dextrose in hyperthyroidism a normal or increased arteriovenous blood sugar difference is found¹ in spite of an increased rate of blood flow. After a carbohydrate meal the rise in the respiratory quotient is higher and the fall is more rapid than normal.² The fall in the inorganic phosphates of the blood is normal.³ Finally, Mirsky and Broh-Kahn⁴ recently obtained direct evidence from experiments on eviscerated rabbits that in hyperthyroidism the utilization of dextrose by the tissues is notably increased.

Opinions differ concerning the nature of the disturbance of carbohydrate metabolism in the hyperthyroid state. Aside from general statements that "toxic" or "nervous" influences are at work, several specific hypotheses have been advanced. Some writers attribute the disturbance to dysfunction of the pancreas or to inhibition of the peripheral action of insulin. Others hold responsible the abnormal mobilization of hepatic glycogen which is caused by stimulation of the adrenals,⁵

or a primary increase in hepatic glycogenolysis.⁶ Still others offer as explanation the inability of the liver to store glycogen because of the toxic effects of thyroxine,² or increased oxidation of carbohydrates in the tissues which leads to a secondary exhaustion of glycogen reserves.⁷ However, none of these hypotheses explain all the abnormal manifestations associated with the metabolism of carbohydrates in hyperthyroidism.

The point of view of the "diabetic" school, which had among its many adherents Naunyn,⁸ Falta,⁹ von Noorden¹⁰ and Murray,¹¹ deserves special attention because it has exerted and still is exerting by far the greatest influence on therapy of disturbed carbohydrate metabolism in hyperthyroidism. In recent years this point of view has been championed by Shpiner,¹² who on the basis of his experiments with animals postulated the possibility of a toxic effect of thyroxine on the islet tissue of the pancreas. Hirschberger¹³ came to the same conclusion from his studies on the dextrose tolerance of patients with hyperthyroidism following the administration of two successive doses of dextrose according to the method of Staub. The prevalent clinical point of view was given by John¹⁴ in the following statement:

I think that the explanation of the disturbed carbohydrate metabolism associated with hyperthyroidism is not found in the state of hyperthyroidism per se, but that it is due rather to some other factor which I believe is a "diabetic anlage" that was present in the patient before the hyperthyroidism developed . . .

Intestinal Absorption of Carbohydrates in Normal, Hyperthyroid and Thyroidectomized Rats

Experimental Condition	Substance Administered	Amount Absorbed in 1 Hour per 100 Gm. of Weight, Mg.
Normal	Dextrose	171 ± 14*
Hyperthyroid	Dextrose	284 ± 30
Thyroidectomized	Dextrose	91 ± 5
Normal	Galactose	187 ± 27
Hyperthyroid	Galactose	273 ± 18
Normal	Starch	126 ± 24
Hyperthyroid	Starch	196 ± 14

* Standard deviation.

The incidence of diabetes in hyperthyroidism is 2.1 per cent. The incidence of diabetes at large is given as 1 per cent. There is thus a 100 per cent increase of diabetes in cases of hyperthyroidism. I am inclined to think that a big factor here is the question of overeating which is automatically brought about by the increased metabolism. . . . This throws a great load on the insulogenic apparatus.

John added that the "nervous regulatory mechanism" and hyperadrenalism may exert some influence.

Aided by a grant from the Christine Breon Fund for Medical Research. From the Department of Medicine, University of California Medical School.

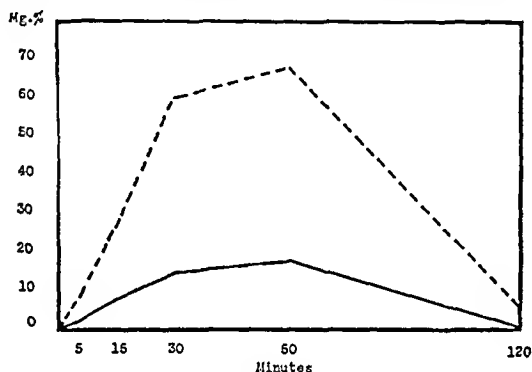
Read before the annual meeting of the Association for the Study of Goiter, Cincinnati, May 22, 1939.

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On the basis of this hypothesis many patients with hyperthyroidism who also have glycosuria, hyperglycemia after meals or high dextrose tolerance curves are subjected either to dietary limitation of carbohydrates or to treatment with insulin, or to both, especially if they show a tendency to acidosis.

Approaching this problem through animal experimentation, my associates and I have shown by direct studies of intestinal absorption in rats that administration of thyroxine has a pronouncedly accelerating influence on the intestinal absorption of utilizable sugars and of starch, as shown in the table. Conversely, thyroidectomy causes marked slowing of the absorption of dextrose from the intestine. A series of experiments reported elsewhere¹⁵ gives evidence that the thyroid hormone influences intestinal absorption chiefly through stimulation of phosphorylation. In phosphorylation a given substance is esterified with phosphoric acid. Phosphorylation takes place in the intestinal mucosa. Through constant transformation of a diffusing substance (for example the transformation of dextrose into hexose-phosphate) the gradient for diffusion of a given substance into the mucosa is kept high and its rate of



Average galactose tolerance curves of ninety-seven persons without thyroid disease (solid line) and 130 patients with hyperthyroidism (broken line).

absorption from the lumen of the intestine is thereby increased. The following conditions were ruled out as factors accelerating intestinal absorption in experimental hyperthyroidism: depletion of carbohydrates, increase in basal metabolism per se, rise in the velocity of the blood flow, intestinal hyperperistalsis, and increased permeability of the intestinal mucosa.

The accelerating influence of the thyroid hormone on intestinal absorption of sugars was observed in clinical hyperthyroidism. A standard amount of galactose was administered to each of 130 patients with this disease, and the galactose curve of the blood¹⁶ was followed in each case. With one exception all these patients had high curves for galactose in the blood. The average galactose curve in hyperthyroidism was more than three times as high as the average curve for this sugar in ten normal volunteers or in eighty-seven patients with diseases other than hyperthyroidism, as shown in the chart. In order to rule out the possibility that the high oral galactose tolerance curves were caused by impaired utilization of galactose, this sugar was administered intravenously and the rate at which it disappeared from the blood stream was determined in patients with hyperthyroidism as compared with normal individuals.

The stimulating effect of the thyroid hormone on absorption of sugar in human beings was confirmed by the observations that the galactose curve returns to normal in patients with hyperthyroidism after they have been subjected to subtotal thyroidectomy, and that very low galactose values are found in the blood of patients with myxedema. Determinations of absorption of galactose as an index of thyroid activity proved to be comparable in reliability to determinations of the basal metabolic rate. In clinical practice the galactose test is found to be particularly useful in patients with hyperthyroidism whose basal metabolic rates are under +20 per cent and in patients whose basal metabolic rates are elevated owing to causes other than hyperthyroidism, such as anxiety states with hyperventilation, cardiac dyspnea and leukemia.

We have seen that only about one half of the patients with hyperthyroidism have abnormally high dextrose tolerance curves while practically all of them show abnormal elevations of the galactose tolerance curves. Since we have shown that the absorption of these two sugars is accelerated to an approximately equal degree and since we know that galactose is not immediately utilized by the tissues but must undergo conversion into dextrose in the liver, this difference is one more proof that the utilization of dextrose is increased in the hyperthyroid organism. It also makes galactose the sugar of choice for diagnostic purposes in diseases of the thyroid gland.

All peculiarities of carbohydrate metabolism in hyperthyroidism are explained satisfactorily by abnormally rapid intestinal absorption of sugars and of starch combined with increased utilization of dextrose by the tissues which leads to depletion of glycogen stores. Increased absorption of carbohydrates accounts for the "diabetic" manifestations of glycosuria, the postprandial hyperglycemia and the high dextrose tolerance curves. Chronic depletion of glycogen stores explains the low fasting respiratory quotient and leads to a compensatory acceleration of fat catabolism which, as in the case of "hunger diabetes," results in incomplete oxidation of fatty acids and brings about acidosis. Increased utilization of carbohydrate accounts for the normal or greater than normal arteriovenous blood sugar difference, postprandial rise in the respiratory quotient, and fall in the inorganic phosphates of the blood, which on the surface appear incompatible with the "diabetic" manifestations of hyperthyroidism mentioned previously. From these considerations it is also easy to see why the onset of hyperthyroidism aggravates a preexisting diabetes.

In the majority of patients with hyperthyroidism in whom diabetes is suspected, accelerated absorption of carbohydrates merely simulates certain manifestations of diabetes mellitus. However, hyperthyroidism may be superimposed on a preexisting diabetes, or the depletion of glycogen reserves and overeating, which characterize the hyperthyroid state, may in a few patients bring out a latent or a previously unsuspected mild diabetes. This explanation given by John of the increased incidence of true diabetes mellitus in patients with hyperthyroidism is supported by the observation also pointed out by John, that the incidence of diabetes in hyperthyroidism does not rise until the beginning of the fifth decade. It may be assumed that at that age the factors precipitating a latent diabetes have exerted their influence for a longer time and that arteriosclerosis has become a contributing factor.

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When diabetes is suspected in a patient suffering from hyperthyroidism, simple and in most cases decisive differential laboratory evidence is the fasting blood sugar, which is, of course, high in diabetes. As a rule it is normal in hyperthyroidism because there is ample time to dispose of the excess sugar in the blood following the evening meal, especially since in this condition the utilization of sugar is increased. Denis, Aub and Minot¹⁷ emphasized that "fasting hyperglycemia is of extremely rare occurrence in hyperthyroidism." This statement is particularly significant since these authors evidently studied patients in whom the disturbance of carbohydrate metabolism was well marked, because they observed alimentary hyperglycemia (following the administration of 100 Gm. of dextrose and 50 Gm. of bread) in all their patients. Rabinowitch¹⁸ confirmed the importance of fasting hyperglycemia in diabetes. However, a moderate elevation of the blood sugar on an emotional basis is sometimes found in nervous patients with hyperthyroidism who become excited by venipuncture, especially if several unsuccessful attempts are made before the needle enters the vein. If in such patients the determination of fasting blood sugar is repeated by a skilled operator after administration of a sedative, normal results are usually obtained. If the fasting blood sugar is still high, the presence or absence of true diabetes can be established in several ways, as pointed out by Marsh¹⁹ and Rabinowitch. In diabetes, in contrast to hyperthyroidism, the following observations apply: (1) Glycosuria corresponds quantitatively to the intake of carbohydrates; (2) the dextrose tolerance curve shows a protracted elevation with the peak at the three hour or even four hour period; (3) the respiratory quotient remains low two hours after a dextrose meal; (4) administration of sugar does not relieve acidosis, and (5) carbohydrates have no protein-sparing action. To these may be added, as discussed previously, the decreased arteriovenous blood sugar difference and the diminished fall in inorganic phosphates of the blood following a carbohydrate meal, both of which are found in diabetes.

Several important therapeutic implications may be derived from the knowledge that the basic abnormalities of carbohydrate metabolism in hyperthyroidism consist of accelerated intestinal absorption and increased oxidation of carbohydrates. In the first place, the presence of glycosuria, postprandial hyperglycemia, or high dextrose tolerance curves in patients with hyperthyroidism does not indicate the coexistence of diabetes and can be disregarded unless there is also a high fasting blood sugar. Second, all patients suffering from hyperthyroidism should receive a high caloric diet with an abundant supply of carbohydrates. In order to compensate for the rapidity of intestinal absorption and for the increased utilization of dextrose in the tissues, it is advisable to divide such a diet into six or more meals given until bedtime. Third, patients with hyperthyroidism should not be subjected to fasting because they have a tendency to acidosis which often develops after relatively short periods of abstinence from food. This consideration is especially important just prior to operative procedures involving general anesthesia, as for instance thyroidectomy, which are a great drain on the glycogen

reserves of the body in general and of the liver in particular. Fourth, intravenous administration of dextrose just before, during and after operations to patients with hyperthyroidism is valuable in lowering the operative mortality.²⁰ Finally, the insulinogenic mechanism of patients with hyperthyroidism who have true diabetes mellitus should be protected as much as possible from the sudden influx of large amounts of sugar after meals. This can be accomplished to some extent by omitting sugars from the high carbohydrate diet and replacing them with starch, which is absorbed more slowly (as we have shown in the table). In addition, such patients need adequate amounts of insulin. The same dietary measures may be used for prophylactic purposes in patients with hyperthyroidism who have a family history of diabetes. On the other hand, insulin should never be prescribed except in cases in which the coexistence of diabetes has been proved.

This study also contributes to a better understanding of the metabolism of carbohydrates in myxedema. It is a matter of general knowledge that dextrose tolerance curves are usually very low in patients with myxedema. In the past this was interpreted to indicate that dextrose is utilized faster than normal.²¹ By studies of direct intestinal absorption in thyroidectomized rats we have shown that removal of the thyroid gland causes marked diminution of absorption of dextrose, as seen in the table. This observation was confirmed clinically by the low values of galactose in the blood of patients with myxedema following oral administration of this sugar.¹⁰ Intravenous administration of galactose to patients with myxedema not only ruled out increased utilization of this sugar but also showed that its removal from the blood is actually slower than normal. Decreased utilization of dextrose in myxedema is in accord with other clinical and biochemical manifestations of this disease, such as a reduction in the endogenous protein metabolism and the energy exchange,²² and probably explains why normal dextrose tolerance curves sometimes are observed in hypothyroidism in spite of decreased intestinal absorption.

No new therapeutic measures have been derived from the knowledge that intestinal absorption of carbohydrates is slowed in hypothyroidism because administration of adequate amounts of thyroid substance corrects this deficiency rapidly and effectively. Experimentally it was shown that intestinal absorption of dextrose is more sensitive to the thyroid hormone than is the basal metabolic rate; doses of thyroxine sufficient to restore normal intestinal absorption raised the basal metabolic rate only halfway to the original normal level.²³

CONCLUSIONS

1. The basic disturbance of carbohydrate metabolism in hyperthyroidism consists of accelerated intestinal absorption of sugars and starch and of increased oxidation of dextrose in the tissues which leads to depletion of glycogen stores.

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2. Glycosuria, postprandial hyperglycemia and high dextrose tolerance curves in patients with hyperthyroidism do not indicate the coexistence of diabetes mellitus unless there is also a high fasting blood sugar.

3. Patients with hyperthyroidism should receive high caloric, high carbohydrate diets divided into frequent feedings.

4. Intravenous administration of dextrose is indicated just before and after thyroidectomy.

5. In myxedema, diminished absorption of carbohydrates accounts for the low sugar tolerance curves.

CLINICAL USE OF IMMUNE HUMAN PLACENTAL GLOBULIN IN CHICAGO

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In 1938 more cases of measles were reported in Chicago than during any year since this disease was made reportable. Table 1 shows that apparently there has been no reduction in the number of cases of measles reported each year over the last twenty-five years. Rather the trend is toward more cases, probably because of better reporting. The mortality, however, has dropped rather steadily from 12.4 per hundred thousand of population in 1913 to 1.1 in 1938.

It should be noted in table 1 that only the years of largest incidence are charted, one might say the epidemic years. In 1938 the case fatality was amazingly low, being 0.1 per cent, whereas in 1913 it was 1.9 per cent. However, during this year the case fatality was low over the entire country. Improved housing, more adequate medical care, better nursing attention, increased use of measles-modifying substances in susceptible contacts, recent use of chemotherapeutic drugs in pneumonias and bronchopneumonias following measles, and perhaps a lessening virulence of the type of measles prevalent in recent years may all have contributed to the reduction in the case fatality rate. Despite the reduced death rates, measles continues to take some human lives, and efforts exerted to save these lives are worth while. Until an active preventive is developed, the increased employment of measles-modifying substances should be encouraged.

In Chicago convalescent measles serum, used as a preventive and modifying substance, is prepared and distributed by the Deutsch Serum Center of the Michael Reese Hospital. Because this material is not always easily available, it was decided to study the effect of immune human globulin,¹ prepared from placental extract, among susceptible contacts. At the same time a comparative study was made with convalescent serum. The control group studied consisted of susceptible contacts who did not receive either immune globulin or serum. Table 2 shows the number of children, by age groups, receiving globulin or serum, and those not receiving any injection.

The group under 1 year consists mostly of children over 6 months of age. In every instance of a child

under 6 months of age, an attempt was made to find out if the mother had had measles, because it is believed that a mother may transmit immunity to measles to the baby through the placenta and that the baby will be thus protected for five, six or seven months after birth.

In Chicago's overcrowded homes of the lower economic levels many babies do not escape measles because of their intimate exposure to the disease. Therefore every child in this group was classed as susceptible since the entire study was made in the poorer sections of the city. Every child under observation was exposed to measles in his own family under his own roof.

METHOD OF STUDY

When measles was reported, a visit was paid to the home by a Health Department investigator, who quarantined the patient and reported the contact status. If there was no private physician in attendance, a field health officer was sent to inject globulin or convalescent serum in the contacts. In every instance possible, if there were several contacts, the health officer inoculated the younger children and employed as controls the older children in the family who gave no history of having had measles.

The health officer made a return visit some time later to note the results and to obtain as much information from the family as possible. He then completed the form shown in table 3.

The health officers engaged in this work were limited to four, so that the results are more reliable than if there were a greater number of observers.

TABLE 1.—Cases of Measles, Deaths and Rates in Chicago, 1913-1938, Inclusive

	Cases Reported							
	1913	1915	1917	1919	1923	1927	1929	1935
Rate	15,132	15,964	19,620	16,075	15,168	17,726	17,714	24,199
per 100,000								
Population	642.68	769.58	763.50	600.95	525.39	554.72	532.33	693.24
	Deaths							
	1913	1915	1917	1919	1923	1927	1929	1935
Rate	292	240	243	197	206	123	166	81
per 100,000								
Population	12.40	9.74	9.46	7.36	7.14	3.85	4.99	2.32
								1.1

TABLE 2.—Age Groups of Children Receiving Globulin Convalescent Serum and No Injection

Age	Material Used		No Injection Given
	Globulin	Serum	
0-1 Yr.	418	218	14
1-3 Yrs.	212	65	115
4-9 Yrs.	45	16	156
10 Yrs. and over	3	0	13
Total	678	299	323

Table 4 shows the dosages of globulin and convalescent serum employed.

Table 5 shows the number of exposed susceptible children who received either globulin or serum and who contracted measles. For comparison, the uninoculated control group is also placed in this table.

In table 5 it is seen that serum offered 21.14 per cent greater protection than globulin, and that globulin

1. The immune globulin was furnished by Lederle Laboratories, Inc., New York.

offered 25.5 per cent greater protection than no injection. Also, it is interesting to note that 26.6 per cent of the exposed susceptible children in the "no injection" group escaped the disease even with measles in their own home.

TABLE 3.—*Information Supplied in Health Officer's Report of Measles Contact Given Globulin*

Original Patient.....						
Name.....		Address.....				
Sex.....	Age.....	Color.....				
Date of Onset.....		Date of Eruption.....				
Contacts (Include Parents)						
Non-Susceptible		Name	Age			
.....				
.....				
.....				
.....				
Susceptible		Name	Age			
.....				
.....				
.....				
.....				
Contacts Injected		Dose Given	Date Reaction			
.....				
.....				
.....				
If susceptible is under 1 year, was baby breast fed?.....						
Did mother of baby have measles?.....						
Contacts Who Developed Measles						
Name	Onset Date	Rash Date	Type of Measles	Symptoms		
				Record from 0 to 4 Plus	Rash	Cough Catarrh Prost.
.....
.....
.....
.....
.....
Complications (if any); Give Name of Child and Describe Nature of Complications						
.....						
Date of all visits.....						
General Remarks						
NOTE: All pertinent information on every globulin assignment is to be filled in on this form when final disposition is made.						
Date When Mailed		Health Officer				

Table 6 shows the number of exposed susceptible children in all three groups who contracted measles and the severity of the disease which developed, whether modified or unmodified.

From table 6 it seems that when globulin or serum was given to susceptible contacts, the two substances acted with almost equal efficiency in the doses used. Among those receiving no injections the percentage of severe cases of measles was almost two and one-half times greater than among those receiving globulin and more than three times greater than among those given convalescent serum. In this table, also, it is interesting to note that of 241 susceptible contacts not receiving any injection and who later developed measles, 76.7 per cent had it in a mild form. However, the measles epidemic of 1938 was, in general, attended with a low case fatality rate.

In table 7 are seen the figures representing both complete and partial protection afforded by globulin and serum. These figures were obtained by adding the number of children with modified measles to the number of susceptible children who did not contract the disease. A modified case of measles represents partial protection,

and if a child does not develop measles it probably means complete protection. For comparison, the group receiving no injection is placed here also. In the last-mentioned group, under the heading of combined protection, are the children who did not have measles together with those who had it in a mild form.

From this table it is seen that with convalescent serum and globulin the percentage of failures to give protection is low. Among the children who received no injection, the percentage classed as failures was more than three times greater than in the globulin group.

In table 8 are recorded the complications occurring in children with measles under observation at the time of the study. Since the complications developed only in those with severe measles, these only are listed.

Table 9 shows the percentage of children who contracted measles and who remained free of rash, cough, other catarrhal symptoms and prostration.

From this table it is seen that children who received convalescent serum and later contracted measles were not as sick as the children who were given globulin and later contracted measles. The children inoculated with globulin were not as sick as those not receiving any injection. Two and six-tenths (2.6) per cent of the uninoculated children had no prostration, as compared with much higher percentages in the other two groups.

TABLE 4.—*Dosages of Globulin and Convalescent Serum Used*

Age	Globulin*	Convalescent Serum
Under 1 year.....	2 cc.	3 cc.
1-2 years.....	2½ cc.	4 cc.
2-3 years.....	2½ cc.	5 cc.
3-4 years.....	2¾ cc.	5 cc.
4-5 years.....	3 cc.	5 cc.
5-6 years.....	3¼ cc.	5 cc.
6 years and over.....	5 cc.

* One-fourth cc. increase in dose for each year.

TABLE 5.—*Number of Susceptible Contacts Who Contracted Measles After an Injection of Either Globulin or Convalescent Serum*

	Globulin	Serum	No Injection
Total number in group.....	678	299	328
Measles developed	325	80	241
Percentage of total.....	47.9	26.76	73.4
Measles did not develop.....	353	219	87
Percentage of total.....	52.1	73.24	26.6

TABLE 6.—*Susceptible Children in Whom Measles Developed, Showing Severity*

	Globulin	Serum	No Injection
Total number contracting measles.	325	80	241
Modified or mild.....	223	74	185
Percentage modified	68.1	92.5	76.7
Unmodified or severe.....	32	6	56
Percentage unmodified	9.9	7.5	23.3

In table 10 is shown the number of children protected by globulin, according to the time interval between exposure and the giving of the injection. Table 11 shows the same for children inoculated with convalescent serum.

Before the sixth day after exposure, 181 children were inoculated with globulin. Of this number, ninety-nine, or 54.6 per cent, did not have measles. After the

sixth day of exposure, 497 were inoculated, of whom 254, or 51.1 per cent, did not have measles. Before the sixth day of exposure, ninety-three children were inoculated with convalescent serum. Of these, sixty-nine, or 74.1 per cent, did not have measles. After the sixth day of exposure, 206 were inoculated. Of these, 150, or 72.8 per cent, did not have measles.

TABLE 7.—*The Combined Protection in the Three Groups*

	Globulin	Serum	No Injection
Total number in group.....	678	299	328
Combined protection	616	293	272
Percentage of combined protection.	95.2	97.9	82.9
Failures (including only unmodified cases)	32	6	56
			(severe cases classified as failures for comparison)
Percentage of failures.....	4.8	2.1	17.1

TABLE 8.—Complications

	Globulin	Serum	No Injection
Number of unmodified cases.....	32	6	56
Number of cases with complications.....	10	2	7
Type of complication:			
Severe bronchitis	6	1	4
Otitis media	2	1	3
Severe diarrhea	1	0	0
Encephalitis	1	0	0

TABLE 9.—Percentage of Children Remaining Free from Various Symptoms of Measles

	Globulin	Serum	No Injection
Free from rash.....	1.6%	2.5%	0.0%
Free from cough.....	5.7%	16.25%	0.82%
Free from catarrh.....	17.0%	17.5%	3.3%
Free from prostration.....	21.1%	20.3%	2.6%

If the date of development of measles in a child in the home as given by parents is accurate, and if exposure of susceptible children is of sufficiently equal degree to make comparison possible, a higher percentage of complete protection should be expected in susceptible children receiving injections before the fifth or sixth day of exposure than after this time. However, onset dates often cannot be accurately ascertained.

It is difficult for parents to know exactly on what day measles develops in a child. In addition, there is a quantitative factor in exposure and susceptibility to measles. Many investigators have found that in a group of children exposed to measles in a hospital who receive a measles-preventive substance, there will be a higher percentage of children completely protected than in a group of susceptible children in the home who are given a measles-preventive substance. This probably occurs because in the home the susceptible child is in contact with the measles for a longer period. Contact between children is much closer in some homes than in others. These factors may help to explain why the expected results in studies made on children at home often do not materialize.

REACTIONS

Reactions from the use of convalescent serum are so unusual that in this study no attempt was made to

note if any reactions occurred. On the other hand, globulin did cause reactions in many children. However, severe reactions were so uncommon that it was felt nothing could be gained from their study. The most common reaction to the globulin was a slight or moderate amount of soreness at the site of injection.

DOSAGE

The dose of globulin used in this study was smaller than that usually recommended. No doubt if larger amounts had been used soon after the exposure, more instances of complete protection would have resulted. The purpose of this study, however, was to evaluate globulin on a large scale basis, and not necessarily to determine the optimum dosage.

It has been repeatedly shown by clinical investigators that the dose of measles-preventive and modifying substances, such as immune globulin or convalescent serum, should be gaged by the following factors: (1) whether the susceptible child is in a hospital or at home, (2) the length of time following exposure, (3) intimacy of exposure, (4) the health status of the susceptible individual and (5) the type of measles prevalent.

SUMMARY

1. Six hundred and seventy-eight (678) susceptible measles contacts were inoculated with immune placental human globulin; 353, or 52.1 per cent, failed to contract measles; 325, or 47.9 per cent, contracted measles. Of the 325 children who had measles, 293, or 90.1 per cent, contracted a modified type of the disease. The number of protected children, including those who failed to have the disease plus those who had the modified type, was 646, or 95.2 per cent, of the 678 children who were susceptible measles contacts.

TABLE 10.—*Number of Days from Onset in Original Case to
Injection of Globulin in Susceptible Children:
Percentage of Group Protected*

Age	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	Total
Under 1 year..	1	5	7	28	38	49	32	39	67	266
	3	6	13	42	56	77	55	62	104	415
1-3 years.....	..	2	3	7	6	13	10	13	17	71
	..	3	8	16	22	39	33	37	54	212
4-9 years.....	1	0	1	2	3	6	1	11
	2	1	9	4	9	11	9	45
10 years.....	2	..	2
	3	..	3
Total.....	1	7	11	35	45	64	45	60	83	333
	3	9	23	59	87	120	97	113	167	615

Before Sixth Day

99, or 54.6%, did not have measles

After Sixth Day

254, or 51.1%, did not have measles

* The numerator is the number of children who did not have measles and the denominator is the total number inoculated.

2. Two hundred and ninety-nine (299) susceptible measles contacts were inoculated with convalescent measles serum; 219, or 73.24 per cent, failed to contract the disease; eighty, or 26.76 per cent, had measles. Of the eighty children who had measles, seventy-four, or 92.5 per cent, contracted a modified type of the disease. Serum, therefore, offered protection to 293 of the 299 children, or 97.9 per cent.

3. Of a control group of 328 susceptible children who did not receive any injection, eighty-seven, or 26.6 per cent, failed to contract the disease; 241, or 73.4 per cent, had measles. Of the 241 who contracted measles, 185, or 76.6 per cent, had a mild form of the disease. For comparison, therefore, the protection in this group may be represented by the children not having measles plus those contracting a mild form of the disease. The protection total was 272 of the 328 in the group, or 82.9 per cent.

4. In a study of the severity of the symptoms in the measles cases occurring in all three groups, it is shown that of the group given globulin and later contracting measles, 21.1 per cent were free from prostration; of the group given serum and later having measles, 26.3 per cent were free from prostration, and of children not receiving any injection and later having measles, only 2.6 per cent remained free from prostration.

TABLE 11.—Number of Days from Onset in Original Case to Injection of Convalescent Serum in Susceptible Children: Percentage of Group Protected

Age	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	Totals
Under 1 year.....	4	11	13	28	21	28	18	57	180
	4	15	14	33	27	34	22	69	218
	0	2	3	5	5	8	4	6	33
1-3 years.....	3	4	4	10	9	12	9	14	65
		2		1	1	0	1	1	6
4-9 years.....	..	3	..	3	3	3	2	2	16
10 years.....
Totals.....	4	15	16	34	27	36	23	64	219
	7	22	18	46	39	49	33	85	299
	Before Sixth Day				After Sixth Day				
	69, or 74.1%, protected				150, or 72.5%, protected				

* The numerator is the number of children who did not have measles and the denominator is the total number inoculated.

5. The time interval after exposure was studied in both the globulin-inoculated and the serum-inoculated group of children. The results obtained were not as expected. The results showed little variation whether the globulin or the serum was given before the fifth or sixth day after exposure or after the fifth or sixth day after exposure. The reasons for this are that (a) onset dates in measles cases occurring in homes often cannot be accurately determined; (b) exposure is more intimate in homes than in hospitals and is more difficult to judge in homes. Expected results, therefore, which may be obtained in hospitals, practically never materialize in the home studies.

CONCLUSIONS

In this study it has been demonstrated that placental globulin (human) can be used with great benefit in the prophylaxis of measles on a city-wide basis. When it is compared with convalescent serum, the serum seems superior, not only because it is more potent but also because reactions are uncommon. However, globulin is more readily available and in a large outbreak would have to be used because of its convenience. The optimum dosage should be determined by the physician attending the patient and the exposed susceptible children.

TRACHOMA TREATED WITH SULFANILAMIDE AND ITS DERIVATIVES

SULFAPYRIDINE AND AZOSULFAMIDE

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Sulfanilamide has been used in the treatment of various bacterial and virus infections with varying success. The causative agent of trachoma is not yet determined, but it is commonly held to be a virus. Recent papers by Loe¹ and Lian² report beneficial results with sulfanilamide in the treatment of trachoma. In February 1939 we started treating trachoma in the outpatient section of the Ophthalmology Department of St. Luke's Hospital No. 2 with sulfanilamide and later with its derivatives azosulfamide (prontosil) and sulfapyridine. This form of treatment of the disease is not well established, and we are presenting our observations in order that they may be added to the reports of others and evaluated, so that this form of treatment of trachoma may be placed on a sound basis.

For purpose of analysis, the cases are divided into two groups: group 1, seventy-five patients receiving sulfanilamide orally, and group 2, twenty patients receiving sulfanilamide and/or its derivatives intramuscularly. Five patients of this group were admitted to the hospital for closer observation and more detailed studies on the effects of the treatment.

GROUP 1: SEVENTY-FIVE PATIENTS TO WHOM SULFANILAMIDE WAS ADMINISTERED ORALLY

The treatment given to group 1 was carried out in the outpatient department. They came under observation every forty-eight to seventy-two hours. The patients in the clinic are mostly refugees, and a few of the more ignorant did not take the drug regularly as specified in the prescription. These did not show as rapid improvement as those who took the drug regularly.

A complete blood count and routine urine examination were done before treatment began and repeated after certain intervals when thought necessary. The patients were warned of the various toxic manifestations of sulfanilamide and told to report immediately if they became ill.

Before sulfanilamide therapy 55 per cent of the patients had had other forms of treatment in this clinic. They were treated with copper sulfate stick, 10 per cent quinine bisulfate, grattage and brossage, chaulmoogra oil, peridectomy and subconjunctival autoserum. The duration of previous treatment varied from twenty-five to 114 days with an average of two months. Many of the patients treated with sulfanilamide were chosen for this study because the former therapy had failed or the improvement was too slow.

Read before the Clinicopathologic Conference at St. Luke's Hospital No. 2, Oct. 4, 1939.

Dr. F. W. King, professor of pharmacology, St. John's University, read and corrected this paper and gave many suggestions.

Dr. F. S. Tsang, head of the Department of Ophthalmology at St. Luke's Hospital No. 2, gave us permission to study these cases.

From the Department of Ophthalmology, St. Luke's Hospital No. 2, and the Department of Pharmacology, Pennsylvania Medical School, St. John's University.

1. Loe, Fred: Sulfanilamide Treatment of Trachoma: Preliminary Report, J. A. M. A. 111: 1371-1372 (Oct. 8) 1938.

2. Sie Boen Lian: Prontosil in Treatment of Trachoma, Geneesk. tijdschr. v. Nederl.-Indië 78: 1058-1065 (May 3) 1938.

Symptoms and Signs of Trachoma.—The subjective symptoms most commonly complained of were, in the order of their frequency, (1) feeling of foreign body, (2) photophobia, (3) lacrimation, (4) pain or eye ache, (5) blurring of vision with marked pannus, (6) discharge, (7) blepharospasm, (8) fatigue, (9) itchiness, (10) heaviness of the lid and (11) blurring of vision without gross pannus.

The objective signs we were concerned with were congestion, papillae, follicles, pannus, infiltrations and corneal ulcers of trachomatous origin. The severity of the lesions varied from trachoma I to trachoma III and pannus from grade *a* to grade *c*.³ In most of these cases there was trachoma II with definite papillary hypertrophy and follicle formation. In 70 per cent of the cases there was very noticeable pannus, and in twelve of them the entire corneal surface was covered by infiltration and vascularization.

Dosage.—The use of sulfanilamide in the treatment of trachoma is so new that we could find no records comparing the effects of various doses. Loc¹ recommends 0.02 Gm. per pound (0.5 Kg.) of body weight. We found this dosage sufficient in some cases but too small for continued improvement in many cases and too high in a few others. Long, Bliss and Feinstone⁴ state that 5.4 Gm. of the drug is required in twenty-four hours by patients weighing from 100 to 150 pounds (from 45 to 68 Kg.) in order to establish and maintain a therapeutically effective blood level with mild or moderately severe infection. We found this dose unnecessarily high in our cases.

Most patients were started on two tablets three or four times daily depending on the body weight, which was usually between 100 and 135 pounds (45 and 61 Kg.). In a few cases it was increased to three tablets or more in each dose and in some was decreased to one tablet four times daily. The total amount of sulfanilamide necessary for improvement varied widely and seemed to have no relative relationship to body weight. One patient received a total dose of 92.7 Gm. (This large dose was given because the patient had a relapse.) Total doses in other cases varied from a maximum of 66.3 Gm. to a minimum of 19.2 Gm.

Clinical Results.—After beginning treatment with sulfanilamide, we found improvement of the subjective symptoms usually noticed after the first twenty-four to forty-eight hours. The disappearance of these symptoms varied, depending on the severity of the case. Usually those having more serious corneal involvement took a longer time to obtain relief. However, this was by no means constant. Hence some thick pannus cleared up rapidly with the disappearance of subjective symptoms, while some with slight corneal involvement required a longer time. Individual response to the drug varied widely. Most of the subjective symptoms disappeared in the latter part of the first week. The maximum time required was fourteen days for all subjective symptoms to clear up. It was found that subjective symptoms improved before improvement of the objective signs could be noticed.

Objectively, we observed that congestion of the conjunctiva became definitely less in some cases on the second or third day and in the majority of them in the first week. The beginning disappearance of follicles and papillae lags a little behind the beginning disappearance

of congestion, but all cases showed definite improvement within the first ten days. Follicles and papillae definitely disappeared from the tarsal conjunctiva, the conjunctival surfaces becoming smooth with distinct blood vessels. However, slight to moderate congestion with occasional follicle and slight papillary hypertrophy still remained at the canthal regions and sometimes at the upper border of the tarsal plate. Improvement in the lower cul-de-sac was not as rapid as that in the upper lid, with congestion and thickened conjunctiva improving very slowly. Continued improvement of these residual papillae, follicles and congestion is very slow and practically imperceptible after long periods of observation—in one case after eight months.

Beginning absorption of pannus was noticed early, especially with grade *a*, in most cases in the first five days. Disappearance or marked improvement of vascularization took place in the first two weeks in practically all cases; in one case in slightly over two weeks, in one in thirty-five days and in one in forty-five days. Incidentally the last was a case of pannus crassus. In five cases sulfanilamide powder was rubbed on the lids in the same manner as boric acid powder is used to see if the congestion and residual follicles at the canthi and upper tarsal border region would disappear. In five control cases no further treatment was given. So far as can be seen, patients were not benefited by sulfanilamide rubbing. However, the subjective symptoms in one relapse improved.

Relapses.—There were one relapse during treatment and two relapses after termination of treatment. Of these three relapses, one occurred after the patient's eye had become comfortable. The dose of sulfanilamide then was reduced from six to four tablets a day. This was followed in two days by lacrimation and blepharospasm. But these symptoms subsided in two days on increasing the dose to eight tablets a day and the patient's improvement was more permanent after that.

The second patient had a relapse after 43.2 Gm. of sulfanilamide had been given, after two weeks of treatment, and he was advised to return for another week's treatment with sulfanilamide. He did not return, however, because he felt entirely comfortable. But one week later he began to have the feeling of a foreign body in his eyes and blurring of vision. Sulfanilamide was rubbed on and these symptoms disappeared subjectively in two days.

The third relapse was that of a technician who came in with trachoma II and pannus *c*. He complained of discharge, photophobia, lacrimation, blepharospasm and great impairment of vision. Under sulfanilamide treatment his eyes became comfortable in one week, and in ten days his pannus disappeared. After three weeks of treatment, the patient having taken 42 Gm. of sulfanilamide, he did not return because, he said, he was cured. A month later he returned to the clinic again with the complaint of red eyes of four days' duration and pannus *b*, corneal ulcer and all the previous symptoms present again. Sulfanilamide was given and in twelve days the condition was brought under control.

Toxic Manifestations.—Practically all our cases showed some toxic manifestations. However, when patients became too uncomfortable, stopping the drug for a day or two was all that was necessary. Toxic symptoms in the order of their frequency were dizziness, numbness of the hands and feet, anorexia, nausea, fatigue, perioral numbness, increase in bowel movements, mild skin eruption, abdominal pain, lumbar ache, pain in the jaw and pain or ache in the knee joint.

3. MacCallan, A. F.: Epidemiology of Trachoma, *Brit. J. Ophth.* 15: 369-411 (July) 1931.

4. Long, P. H.; Bliss, Eleanor A., and Feinstone, W. H.: Mode of Action, Clinical Use and Toxic Manifestations of Sulfanilamide: Further Observations, *J. A. M. A.* 112: 115-121 (Jan. 14) 1939.

Four patients in the series of seventy-five could not go on with the sulfanilamide treatment owing to marked anorexia, malaise and general discomfort.⁵

GROUP 2: TWENTY PATIENTS TREATED INTRAMUSCULARLY WITH SULFANILAMIDE AND ITS DERIVATIVES.

Our results with sulfanilamide given orally demonstrated to us the effectiveness of this form of treatment in trachoma. However, we experienced some difficulties and found that sulfanilamide presented the following disadvantages: 1. Large doses were necessary for improvement in most cases. 2. These large doses gave toxic symptoms. 3. Owing to irregularity or uncertainty of absorption, it was difficult to standardize the dose. 4. Many of our patients were unable to follow the directions strictly when taking the drug over a long period (three or four weeks). We searched for other methods of administration of the drug and found that Somers⁶ reported that a fine suspension of sulfapyridine in distilled water given intramuscularly and intrathecally in cases of cerebrospinal fever had been successful. Kuo⁷ gave it intramuscularly in 0.8 per cent sodium hydroxide in the treatment of pneumonia.

In the treatment of trachoma, in which the action of the drug should be present for three or four weeks, the formation of a drug depot in the gluteal muscles, where the insoluble substance would be absorbed very slowly and continuously, seemed rational. This form of administration presented other advantages: smaller doses could be used with less chances of toxic manifestations, and dosage could be more accurate.

Preparations Used.—We found that sulfanilamide suspended in physiologic solution of sodium chloride logged up even our largest bore of intramuscular needles. We were unable to produce a suspension fine enough either with triturated tablets or with a pure crystalline product.

We then tried a preparation of sulfapyridine and found it very satisfactory, as it formed a milky, easily injectable suspension. The injection, however, was painful. We then used olive oil as a vehicle, adding ethyl aminobenzoate, 2 per cent giving a practically painless injection. Sulfanilamide could also be given in oil, but the clinical results were not as satisfactory as those of sulfapyridine.

Sulfapyridine and sulfanilamide were given in a 10 per cent suspension. Higher concentration gave rise to difficulty in injection. We also tried giving sulfapyridine suspended in 0.8 per cent sodium hydroxide but found that it had no special advantages over the oil preparation and was much more painful.

Therefore in most of the cases recorded in this paper a 10 per cent olive oil suspension of sulfanilamide or sulfapyridine with 2 per cent ethyl aminobenzoate was used.

Clinical Observations.—A. Cases in the Outpatient Department: Fifteen cases of trachoma were treated in

the eye department with intramuscular injections of either sulfanilamide or sulfapyridine or both. In these cases no attempt was made to continue injections after subjective complaints and corneal lesions had markedly improved. These fifteen cases are subdivided into three groups according to the drugs administered.

1. Sulfanilamide. Four cases. Each injection consisted of 3 Gm. of sulfanilamide suspended in 30 cc. of olive oil.

Two cases of trachoma IIa with pannus a and trachoma IIb with pannus c respectively showed satisfactory improvement subjectively and objectively forty-eight hours after injection, in one case with complete ocular comfort in four days. In each there was one injection.

One case of trachoma IIIa with pannus c showed only moderate improvement after forty-eight hours and improvement was noticed after a second injection five days later.

2. Sulfapyridine. Nine cases. There were two cases of trachoma I, six cases of trachoma II and one case of trachoma IIIb. Except in one case, there was pannus varying from grade a to grade c. All cases but one (a case of trachoma IIb with pannus a) showed marked improvement within forty-eight hours after injection, with the pannus clearing up rapidly and improvement in the palpebral conjunctival lesions more marked than in the first group.

In all these cases 3 Gm. of sulfapyridine in oil was given in each injection, and the number of injections in each case varied from one to three. Improvement progressed between injections, which were given at intervals of about seven to ten days depending on the progress noted.

3. Sulfanilamide followed by sulfapyridine. Three cases. Two cases did not respond to sulfanilamide fast enough and sulfapyridine was given a few days later, followed by marked objective improvement and disappearance of subjective complaints in ten days.

One case of trachoma IIIa with pannus c responded well to sulfanilamide, subjective complaints disappearing within eight days after two injections of sulfanilamide of 2 Gm. each. Two injections of sulfapyridine of 3 Gm. each were given later, and progressive improvement of condition was observed with the lids becoming pale and smooth except at the canthal regions and the cornea clear in thirty-five days of treatment.

B. Cases in the Hospital: Five patients were admitted to the hospital for more detailed and prolonged observation and for blood studies:

CASE 1.—W. A. N., a woman aged 47, weighing 138 pounds (63 Kg.), complained of blepharospasm, photophobia, itchiness, lacrimation, discharge and much pain in the left eye.

Examination showed trachoma IIb in each eye with gelatinous confluence of follicles and a much thickened lid, which was everted only with difficulty. Congestion was moderate. Pannus tenuis was present in the right eye, covering two thirds of the cornea, and pannus crassus with connective tissue degeneration and a large, fairly deep ulcer measuring 3 by 4 mm. in the lower half of the left eye.

She was given boric acid wash in each eye three times daily, 1 per cent atropine three times daily in the left eye and one injection of sulfapyridine 3 Gm. suspended in 30 cc. of physiologic solution of sodium chloride intramuscularly on admission. Improvement was definitely noticed in thirty-six hours with the itching gone and all other complaints improved. The congested appearance of the eye was definitely better. In nine days the ulcer in the left eye was healed and the right eye completely comfortable with the pannus tenuis gone. In another week the left eye was comfortable with steady progress

5. In this connection it may be of interest to note that azosulfamide in 0.5 Gm. tablets was given to these four patients and was well tolerated. Azosulfamide tablets were also given to two other patients who had been treated with sulfanilamide and after slight initial improvement showed no further progress, even with large doses. On changing the treatment to azosulfamide they became symptom free with marked objective improvement. Two other patients were treated with azosulfamide tablets alone with very satisfactory results. Our general impression is that azosulfamide is as effective as sulfanilamide in the treatment of trachoma and may be tried when sulfanilamide is not well tolerated or when the clinical response of the patient to even large doses of sulfanilamide is not satisfactory.

6. Somers, R. B. U.: M. & B. 693 in *Cerebrospinal Fever: Review of 143 Cases Treated Under Field Conditions*, *Lancet* 1: 921-922 (April 22), 1939.

7. Kuo, P. T.: Personal communication to the authors.

thinning of the pannus crassus and absorption of degenerated connective tissue, leaving behind only a faint vascular remnant in the cornea thirty-five days after the first injection. After another fifteen days in the hospital the patient was discharged to the outpatient department for further observation, symptom free with the corneal trachoma healed and the tarsal con-

TABLE 1.—Sulfanilamide Level in Blood After Intramuscular Injection

Case	Dose, Gm.	Blood Level, Mg. per 100 Cc.													
		Hours							Days						
		1/4	1	6	12	1	2	3	4	5	6	7			
1	3.0	2.69	3.37	4.34	3.47	2.00	3.68	2.00	0	0			
2	3.0	2.61	1.32	1.06	0.90	0.83	Trace			
3	3.0	1.48	2.01	1.11	0.83	Trace			
4	5.0	1.15	0			
5	3.0	2.68	1.20	0.77			

unctiva very much thinner; only a few flat follicles and fine papillae were scattered about, mostly at the canthal regions. Injections of 3 Gm. each of sulfapyridine suspended in physiologic solution of sodium chloride were given intramuscularly on the first, fourth, twelfth, twenty-first, twenty-seventh, thirty-eighth and fiftieth day of residence, a total of 21 Gm. (No further improvement was noted after the last two injections.)

CASE 2.—Y. K. M., aged 30, weighing 125 pounds (57 Kg.), complained of marked blepharospasm, photophobia, lacerimation, discharge and pain in the right eye.

Examination showed a congested palpebral conjunctiva with thickened tarsal plate and trachoma IIb. Pannus *a* was present in the right eye with a large deep horseshoe shape ulcer distal to the pannus.

The patient was given sulfanilamide 3 Gm. in oil intramuscularly on admission, with boric acid wash and 1 per cent atropine in the right eye. In four days all complaints ceased, with disappearance of the pannus and healing of the corneal

four hours there was much less pain, with the patient able to open the eyes wide and the intensity of congestion and pannus markedly reduced. Improvement progressed and the ulcer healed on the fourth day after injection. Three more days and the patient became symptom free. On the day of discharge the palpebral conjunctiva was pale and the cornea clear.

Two 3 Gm. injections of sulfapyridine were given altogether, one given in oil on admission and the second one suspended in 0.8 per cent sodium hydroxide fourteen days later.

CASE 4.—C. C. G., aged 20, weighing 120 pounds (54 Kg.), complained of photophobia, discharge, lacerimation, itchiness, fatigue, blurring of vision and the feeling of a foreign body. Examination showed a diffusely congested thickened gelatinous palpebral conjunctiva with indistinct scarring at the upper tarsal border. Pannus grade *c* was present in the right eye and pannus grade *b* of chronic congestive type with infiltration staining with fluorescein in the left eye.

Sulfapyridine was injected on admission. The patient in the first thirty-six hours complained of increased blurring of vision with more lacerimation and pain and the infiltration getting larger. The condition, however, improved markedly the next day, with congestion much decreased and the eyes becoming comfortable six days after admission and lesions improving progressively. The pannus became very pale and sparse but refused to disappear altogether until peridectomy had been done.

Intramuscular injections of 3 Gm. of sulfapyridine in physiologic solution of sodium chloride and one intramuscular injection of sulfapyridine in olive oil were given on the first, fifth, ninth, thirteenth, seventeenth, twentieth and thirtieth day of residence.

The patient was discharged to the outpatient department after observation in the ward for thirty-eight days. The gelatinous condition of the conjunctiva was gone; a fine network of scarring was visible, and there was slight congestion at the canthal region with no definite follicles or papillae. The pannus was entirely gone and the cornea somewhat hazy from scar tissue.

TABLE 2.—Sulfapyridine Level in Blood After Intramuscular Injection

Case	Dose, Gm.	Blood Level, Mg. per 100 Cc.																		
		Hours									Days									
		1/4	1	6	12	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	3.0 in NaCl	3.57	2.37	2.50	3.04	3.87	2.92	2.60	2.01	2.80	3.20	2.80	2.17	1.85	1.85	0.50	0	0	0
2	3.0 in oil	2.17	3.11	4.71	5.00	5.23	3.94	2.95	3.01	3.33	3.12	3.25	3.07	5.72	3.25	2.50	1.50	0
3	3.0 in 0.8% NaOH	2.85	2.75	3.20	3.15	2.17	2.41	2.72	2.56	2.35	3.07
4	3.0 in oil	4.50	4.40	4.00	3.80	3.37	3.10	2.61	2.40	2.80	3.07	3.40	2.90	3.31	4.54	2.50
5	3.0 in 0.8% NaOH	3.20	2.89	3.06	2.85	2.30	2.46	2.40	2.24	2.80	2.50	2.40	2.31	1.54	Trace
6	2.0 in oil	3.17	2.37	2.95	2.52	2.85	3.00	3.10	3.21	2.83	3.50	4.89	3.96	2.01	2.77	1.58
7	2.0 in oil	2.86	2.73	1.90
8	3.5 in oil	2.67	2.73	3.00	3.50	2.47	3.03	2.20
9	4.5 in 0.8% NaOH	4.66	2.94	3.75	3.19	2.75
10	2.0 in oil	2.46	2.30	2.14	2.70	2.50	0
11	3.5 in 0.8% NaOH	4.49	3.68	2.91	2.50
12	3.0 in oil	2.40

deer. Congestion of the palpebral conjunctiva gradually subsided and on discharge, nineteen days after admission, after two 3 Gm. injections of sulfanilamide ten days apart, the palpebral conjunctiva was pale except for some moderate congestion at the canthi with some unevenness of the surface. No definite follicles or papillae were seen; the cornea was clear of vascularization and infiltration, with the former ulcer now an excavation. Except for this optical defect the eyes felt quite comfortable.

CASE 3.—T. I. P., aged 64 and weighing 80 pounds (36 Kg.), complained of blepharospasm and photophobia in each eye with pain in the right eye.

Examination showed the palpebral conjunctiva moderately congested. In the right eye there was trachoma IIb with pannus tenuis with infiltration taking a fluorescein stain; the left eye showed pannus vasculosus with a large deep horseshoe ulcer. Boric acid wash, 4 per cent vitamin A ointment⁸ and 1 per cent atropine were given locally in each eye and 3 Gm. of sulfapyridine in oil intramuscularly on admission. In twenty-

8. Ointment made from vitamin A concentrate.

CASE 5.—T. K. T., aged 13, weighing 63 pounds (29 Kg.), complained of lacerimation, photophobia and blepharospasm.

Examination showed trachoma IIb with a large number of prominent follicles all over; the palpebral conjunctiva was diffusely congested. Pannus *a* was present in the right eye and pannus *b* with infiltration in the left eye.

Sulfapyridine 2 Gm. in physiologic solution of sodium chloride was given intramuscularly on admission. Within eight days the eyes became completely comfortable with the pannus entirely gone. Follicles progressively became smaller until on the day of discharge, in marked contrast to the condition of the palpebral conjunctiva on admission, no more were left on the tarsal conjunctiva and only some roughness and three or four flattened follicles with slight congestion were left in the canthal region. The lower cul-de-sac was less infiltrated but the conjunctival structures remained indistinct. Sulfapyridine injections of 2 Gm. each were given on the first, fifth, tenth, fourteenth, nineteenth, twenty-third, twenty-seventh, thirty-third, thirty-ninth, fifty-second and sixty-fifth day of residence, a total of 22 Gm. No further progress was noted after the seventh injection.

Drug Reactions.—In about 80 per cent of our cases, pain and tenderness at the site of injection was noticed from six to twelve hours after injection, accompanied by fever, with a temperature ranging from 99.6 to 103 F., the former requiring from two to four days to disappear and the latter from twelve to twenty-four hours. There were in some cases headache, malaise and nausea, but only during the fever reaction. Patients complained only of some local discomfort at the site of injection but not of any of the toxic manifestations evinced by the first series of trachoma patients, who were taking sulfanilamide orally. No abscess formation ever occurred at the site of injection.

Repeated complete blood counts done in the hospital cases showed no signs of anemia, and except in one case, with a drop of 15 per cent neutrophils without leukopenia, there was no indication of danger of granulocytopenia. Hematuria did not occur.

Drug Level in Blood.—In several cases the drug level in the blood was determined according to the method of Werner⁹ in an attempt to find out whether a drug depot could actually be maintained or not and to ascertain the approximate minimal therapeutic level of the drug in the blood. Data are given in terms of milligrams of total sulfanilamide per hundred cubic centimeters. The tables and the chart show the results for our hospitalized patients and some of our outpatients who were receiving the drug intramuscularly.

Dosage.—From our clinical observations and from our blood level estimations it seems to us that from 2 to 5 Gm., depending on the body weight of the patient, of sulfanilamide or sulfapyridine should be administered in each intramuscular injection. Generally speaking, for sulfanilamide one injection every four days is necessary and for sulfapyridine one injection every seven to ten days. Clinical response of the patients should be taken into consideration in determining the dose. Injection should be given until the patient is symptom free, the corneal lesions gone and the pathologic change of the palpebral conjunctiva much improved. For these results from two to six injections were all we found necessary; prolonged treatment did not give further improvement and is therefore undesirable.

COMMENT

The results of our studies show sulfanilamide and its derivatives to be of definite therapeutic value against trachoma, especially in its acute stages. They act more markedly and more rapidly on the cornea as shown by the more rapid disappearance of the pannus in comparison with the follicles and papillae. The rapidity with which pannus is brought under control and ulcers healed saves the patient from otherwise increased visual disability.

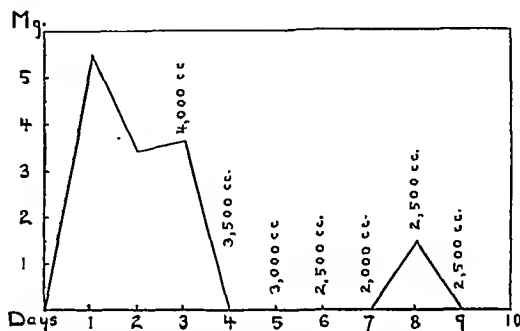
From the public health point of view, as compared with other treatments, the shorter time in stopping discharge and lacrimation is very important in decreasing the chance of spread of the disease, since trachoma is most contagious when there is much discharge and lacrimation.

Our observations have shown that relapses can occur even during treatment and that an increase in dose may be necessary in these cases.

Our experience with intramuscular administration of sulfanilamide and sulfapyridine showed that sulfapyridine is more effective, probably owing to a higher and more prolonged blood level, than a similar dose of sulf-

anilamide (tables 1 and 2). Two patients not discussed in this paper responded much more rapidly to sulfapyridine by mouth after having had sulfanilamide orally. Sulfapyridine may have a more specific effect on the trachoma virus, although more study is necessary to enable us to draw a definite conclusion.

Long¹⁰ warned against the intramuscular administration of an oil preparation of sulfanilamide on the grounds that with a severe reaction rapid elimination of the drug would be impossible. However, in all cases in which severe toxic reactions have been reported,¹¹ much larger doses in a shorter period of time have been used, consequently with a much higher blood level as compared with the amount suggested by us. Besides, as shown in the chart, the drug level in our cases could be depressed to zero by forcing fluid. We think therefore that, with the small amount of drug used and the ease by which the drug level could be lowered, administration by intramuscular injections of sulfanilamide or



Level of sulfapyridine in the blood of a patient given 4 Gm. intramuscularly, followed by forced fluids begun on the third day. The drug level is given in milligrams per hundred cubic centimeters and the amount of fluid in cubic centimeters administered in twenty-four hours.

sulfapyridine in oil is as safe as oral administration if not more so because of slower absorption and is much more economical.

SUMMARY AND CONCLUSIONS

1. Studies on treatment of trachoma with sulfanilamide and its derivatives administered orally to seventy-five patients and intramuscularly in the form of a fine suspension in oil to twenty patients were made in St. Luke's Hospital No. 2.

2. They were found to be definitely effective against trachoma in stages I, II and III, being most useful in eliminating subjective complaints and in checking and healing pannus and corneal ulcer. Pathologic conditions in the palpebral conjunctiva were improved markedly but always remained in the canthal regions. The upper and lower cul-de-sac were not much influenced by prolonged oral or intramuscular administration of the drugs.

3. Intramuscular administration of sulfanilamide suspended in oil and especially of sulfapyridine has, besides the therapeutic effectiveness of the oral administration, the advantage of prolonged action, decreased dosage, lack of toxic manifestations and increased ease in con-

10. Long, P. H.: Oily Suspension of Sulfanilamide, *Lancet* 1: 60 (Jan. 7) 1939.

11. Coxon, R. V., and Forbes, J. R.: Agranulocytic Angina Following Administration of M. & B. 693, *Lancet* 2: 1412 (Dec. 17) 1938. Barnett, H. L.; Hartmann, A. F.; Ferley, A. M., and Ruhoff, M. B.: Treatment of Pneumococcal Infections in Infants and Children with Sulfapyridine, *J. A. M. A.* 112: 518-527 (Feb. 11) 1939. Johnston, F. D.: Agranulocytosis Following Treatment with M. & B. 693, *Lancet* 2: 1200 (Nov. 19) 1938. Sutherland, M. E.: Agranulocytosis Following Administration of M. & B. 693, *ibid.* 1: 1208 (May 27) 1939. Sackett, H. A., and Price, A. E.: Fatal Granulocytopenia Following Administration of Sulfanilamide, *J. A. M. A.* 112: 823-828 (March 4) 1939. Harvey, A. M., and Janeway, C. A.: Development of Acute Hemolytic Anemia During Administration of Sulfanilamide (Para-Aminobenzenesulfonamide), *ibid.* 109: 12-16 (July 3) 1937.

9. Werner, A. E. A.: Estimation of Sulfanilamide in Biological Fluids, *Lancet* 1: 18-20 (Jan. 7) 1939.

trolling and managing patients. The disadvantage lies in the pain and transitory fever the injection causes, although they are never severe enough to incapacitate the patient.

4. Blood estimations show that sulfanilamide administered intramuscularly is present in the blood for approximately four days, while sulfapyridine remains in the blood from ten to fourteen days, whether they are suspended in physiologic solution of sodium chloride, olive oil or 0.8 per cent sodium hydroxide. The minimum therapeutic level appears to be between 2 and 2.5 mg. per hundred cubic centimeters.

5. In the oral administration of the drug, the daily dose of 0.02 Gm. per pound of body weight may be used in all cases with the reservation that it may be either increased or decreased during the course of treatment according to the clinical response of the patient; slow or no response of some patients to the drug may be corrected in practically all cases by increase in the dose. In a few cases, changing to azosulfamide or to sulfapyridine proved effective. The duration of treatment varied from two to four weeks.

In the intramuscular administration of the drug, the dose is from 2 to 5 Gm. per injection, depending on the weight of the patient, sulfanilamide being given every four days and sulfapyridine every seven to ten days. From two to six injections are all that are necessary; more are undesirable, since improvement further than that just described has never been observed.

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LYMPHOSARCOMA

A STUDY OF 196 CASES WITH BIOPSY

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(Concluded from page 23)

TREATMENT

It was but part of a natural course of events which caused irradiation to supplant surgical methods almost entirely in the treatment of lymphosarcoma, for in no other tumor process is there so startling a response to this mode of therapy. In general lymphosarcoma is extremely radiosensitive, and it is not surprising to observe a bulky tumor mass regress to half its size after a few days of treatment and completely disappear within a week. Recurrences in areas adequately treated rarely occur, the new evidence of disease being found elsewhere.

With several types of irradiation available at the Memorial Hospital, various methods of treatment and their combinations have been employed over a twenty year period. Forty-nine per cent of the patients were treated by x-rays alone generated at from 140 to 200 kilovolts. Target-skin distances varied from 35 to 100 cm., depending on the depth of the tumor beneath the skin surface. Filtration also varied considerably from none at all to 0.5 mm. of copper. The area of any field treated was uniformly planned so as to encompass well the tumor known to be present, no attempt being made in a routine way to apply so-called prophylactic treatment to adjacent, clinically uninvolved node groups or tissue with the purpose of destroying embolic deposits presumed rather than known to be present.

Dosage has been purposely varied from 100 to 800 roentgens per individual treatment, the interval between treatments being roughly proportional to the size of the single dose to allow for skin recovery and varying, therefore, from one to seven days. The total amount delivered to any area was determined as treatment proceeded by the rate and degree of tumor regression as well as by the condition of the skin. Twelve per cent of patients were treated by radium element or radon. In the majority of these the 4 Gm. radium element pack was used at from 6 to 10 cm. distance. In an occasional instance this was supplemented by interstitial implantation of gold-filtered radon seeds. Individual treatments varied in amount from 4,000 to 10,000 milligram hours, the same considerations maintaining as in using x-rays with regard to the time permitted to elapse between treatments and the total dose transmitted to any given area. Thirteen per cent of patients were given both x-rays (from 140 to 200 kilovolts) and the radium element pack treatment.

Any disease in which the rapidity and extent of growth may vary so markedly and whose manifestations are so protean requires the strictest individualization of treatment. Consequently, no definite pattern for the management of these patients can be laid down. In an attempt to convey an approximate idea of what has been done, however, the course of the entire group has been calculated on the basis of averages. It is hoped that the amalgamation of such a large number of proved cases as is here presented may justify this otherwise dangerous and frequently misleading procedure, and it must constantly be borne in mind that only in the most general sense can such figures be applied to individual cases.

A hypothetical average patient therefore received a total of twenty-four treatments (x-rays, element pack, or both) with an average interval of two or three days between them. These twenty-four treatments were given in an average of three separate courses, with an interval of about thirteen weeks elapsing between two successive courses. It might here be repeated that the principle determining a new course of therapy was in all instances clinical evidence of recurrent or metastatic disease and that in no instance was prophylactic treatment given. Therefore the number of courses reflects the activity of disease in the average case rather than a degree of ambition in applying treatment. Such a course might consist of a single or several treatments to one or more areas. The total number of areas treated averaged six or seven, with about four treatments per area. In respect to dosage, the average patient received a little more than 400 roentgens¹⁰ per treatment, about 1,600 roentgens per area, and about 3,500 roentgens per course. The average radium treatment consisted of from 7,000 to 7,500 milligram hours, each area receiving about 35,000 milligram hours, and about 40,000 milligram hours constituting the average dose per course.¹¹

Eleven per cent of the patients received Heublein total radiation treatment. The average dose per treatment in the entire group was 125 roentgens. This form of therapy was usually reserved for those with generalized lymphosarcoma or for those in whom the disease by its aggressiveness threatened soon to become widespread. Therefore in later judgment of this form of treatment consideration must be given to the unfavorable type of disease assigned thereto.

10. This represents roentgens in air and not tissue dosage.

11. The much smaller number of cases in this group (twenty-one) makes any generalization very uncertain.

Surgical therapy was initially employed in 15.3 per cent of cases, with the intention of thereby effecting a cure. It consequently follows that any patient for whom surgical treatment became necessary as a result of disease complication such as intestinal obstruction is not included in this group. It also follows that in each of

TABLE 4.—End Results in Lymphosarcoma After Five Years or More

Total number of cases.....	196
Indeterminate group	
Dead of other causes without recurrence }.....	6
Lost track of without recurrence }.....	53
Patients dying of disease 1934-1938 *.....	64
Determinate group	
Total number minus indeterminate group.....	132
Failures	
Dead of lymphosarcoma }.....	111
Lost track of with disease }.....	
Successful results	
Patients surviving 5 or more years.....	21 (15.9%)
End results after five years	
Patients dying of disease or living with recurrence after 5 years.....	7 (5.3%)
Patients living and well after 5 years (apparently cured).....	14 (10.6%)

* Indeterminate only from standpoint of five year end results.

the cases just cited the surgical procedure was extirpative in type, as much of the tumor being removed as was possible when complete removal could not be accomplished. This involved either excision of an extra-nodal primary lesion or a node dissection or both.

About one fifth of the surgically treated patients received no other form of therapy. The remainder all received postoperative external irradiation, either radium or x-rays, given regardless of the absence of clinical disease. This might be regarded then as the only type of case in which prophylactic irradiation was given. Five and five tenths per cent of patients received injections of erysipelas and prodigious toxins (Coley ^{11a}) supplementary to irradiation, operation or both.

Transfusions were resorted to when anemia or leukopenia became marked following irradiation, the rationale being simply to tide the patient over a critical period when diminished resistance might throw wide open the door to a fatal infection. This occasionally appeared to be quite successful. In instances, however, in which the disease has become uncontrollable and is rapidly advancing, blood infusion becomes simply a gesture and has no practical value.

PROGNOSIS AND RESULTS OF TREATMENT

Adopting the method of reporting end results suggested recently by Martin, with slight modifications (tables 4 and 5), there are in the determinate group 132 patients of whom twenty-one have survived five or more years, a five year survival rate, therefore, of 15.9 per cent. Desjardins and Ford reported an 11 per cent five year survival rate in 1923. Of our survivors fourteen (10.6 per cent) are living and are apparently cured, five (5.3 per cent) died of their disease at least five years after treatment, and two are living with active disease still present. Reports of from 30 to 35 per cent five year cases (Leucutia, ¹² Jutras ¹³) with the present

day methods of treatment are open to question. A more critical review of pathologic material might well reduce such optimistic figures.

In the course of studying the entire group of cases here presented it became strikingly apparent that probably the single most important factor determining success or failure in lymphosarcoma lay in some inherent quality of the disease which as yet it is impossible to evaluate. The histologic picture, so helpful in prognosticating the course of many tumors, is of little aid here. One cannot predict on the basis of histology which of two clinically similar cases is apt suddenly to become generalized and which will remain localized for a considerable period. In carefully reviewing the microscopic slides of cured patients no explanation for their favorable outcome could be obtained; in fact several presented as wild a picture as could be imagined. In general the giant follicle lymphomas run a less rapid course, one of nine patients being alive and well and the remainder having survived for an average of forty-two months (more than twice that of the general group). Of the patients having tumors of the small cell type (malignant lymphocytoma) none are living but the average duration of life was 18.6 months (about the same as that of the general group).

The clinical setting is slightly more helpful. Of the twenty-one patients surviving only four had more than two contiguous areas of involvement at the time of admission, so that it may be stated that survivals will probably be secured from the group arriving with clinically early disease. However, of patients eventually dying from disease, those whose disease was considered early at the time of admission (one or two areas of

TABLE 5.—Summary of Patients Surviving Five Years or More (Twenty-One)

1. Incidence:	
Sex: Males.....	11
Females.....	10
Age (average).....	46 years
2. Average duration of symptoms before treatment.....	12.0 months
3. Extranodal primary.....	9 cases—(43%)
(Involving one of the head structures.....)	6 cases)
4. Average number of areas involved on admission.....	1.5
(4 patients had 3 or 4 areas involved)	
5. Prognosis Table:	
Determinate group.....	132 cases
Five year survivals.....	21 cases—(15.9%)
Apparently cured after 5 years.....	14 cases—(10.6%)
Died of disease after 5 years.....	5 cases—(4.4%)
Living with disease.....	2 cases—(1.5%)
6. Treatment:	
Surgical alone.....	1 } All living and well
Surgical plus irradiation.....	5 }
X-rays alone.....	11 } 6 died of disease } 2 had supplemen-
Radium alone.....	0 }
X-rays plus radium.....	4 } 1 died of disease
	21 }
7. Main Treatment Factors:	
Average roentgens per treatment.....	410
Average roentgens per area.....	1,770

involvement) outlived those who were considered to have generalized involvement (three or more areas) by only one month.

When the disease begins in one of the cranial structures the prognosis appears to be somewhat better, twenty-three per cent of patients surviving five or more years and 15.4 per cent being apparently cured.

The occasion of a primary site in the gastrointestinal tract, regardless of sporadic reports of cures, seems to carry with it an unfavorable outlook. None of the

11a. Coley, W. B.: End Results in Hodgkin's Disease and Lymphosarcoma, Treated by the Mixed Toxins of Erysipelas and Bacillus Prodigious, Alone or Combined with Radiation, Ann. Surg. 88: 641 (Oct.) 1928.
12. Leucutia, Traian: Irradiation in Lymphosarcoma, Hodgkin's Disease and Leukemia, Am. J. M. Sc. 188: 612 (Nov.) 1934.
13. Jutras, Albert: Protracted Roentgen Therapy of Pharyngeal Lymphosarcoma, Am. J. Roentgenol. 39: 792 (May) 1938.

patients whose stomach or small intestine was involved lived five years, the average survival period being 6.6 months.

Of the patients in whom a leukemic or pseudo-leukemic blood picture was superimposed none survived five years, but the average survival from time of onset until death was 24.2 months, no shorter than for

the lymphosarcoma group as a whole.

The age of the patient appears somehow to exert considerable influence on the subsequent course (fig. 10), those under 30 years of age tending to experience a much more acute course and having about half the life expectancy of those over 30. After 50 years of age the life expectancy drops off somewhat, probably as a result of the increasing influence of complicating degenerative systemic changes. Since quantitatively treatment was about the same for

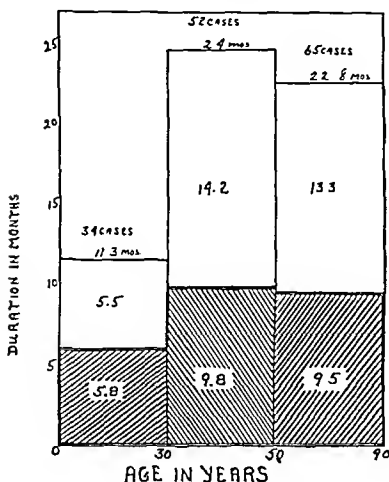


Fig. 10.—Influence of age on the course of the disease, the relatively greater influence of treatment in patients over 30 years of age and the average life span from onset of symptoms till death. The average duration of symptoms until initiation of treatment (shaded) was 8.7 months for all ages. The average duration of treatment until death (white) was 11.8 months for all ages. The average duration of the disease was 20.5 months.

all of these age groups, the explanation must be in the disease itself. The average age of the patients surviving five or more years was 46 years, about the same as that of the entire group. Only a single patient under the age of 30 survived.

It would appear to be a matter of the utmost importance in any disease offering so dismal an outlook to attempt to form some practical opinion of the relative worth of the several methods of treatment employed (table 6). Of sixty "determinate" patients treated by x-rays alone nine, or 15 per cent, survived five or more years. Five of these (8.3 per cent) are apparently cured; two subsequently died of disease and two are living with disease still present. Four (19 per cent) of twenty-one patients treated by both x-rays and radium (interstitially or by element pack) survived five years, but one later died of disease. Of seventeen patients treated by means of the 4 Gm. element pack alone, none have survived five years. There were ten determinate patients who received Heublein whole body irradiation following initial local irradiation or surgical treatment and of these two survived five years but eventually died of disease.

In summary, then, 108 patients were treated by some method of irradiation of whom fifteen (13.9 per cent) survived five or more years but of whom only eight (7.4 per cent) are apparently cured.

Twenty-five determinate patients were initially subjected to some extirpative surgical procedure: removal of an extranodal primary site (such as tonsil, breast or ileum) in eleven; node dissection in twelve, and removal of both an extranodal primary and an adjacent involved node group in two. With all but a few of these patients surgical treatment was shortly followed by local external irradiation given prophylactically. Of

these patients six (24 per cent) are living five or more years later and all are apparently cured. A group of sixty-two patients on admission were considered to have a comparable amount of clinical disease, though in some instances not as anatomically accessible, and were treated by some form of radiation. Of these 16 per cent survived five years but only 8 per cent are apparently cured. The small size of these two groups prohibits any definite conclusions but certainly encourages further trial of a combined surgical and radiologic approach in these early cases.

It should be pointed out that many of the surgically treated patients were operated on in smaller hospitals by surgeons who were first aware of the prevailing condition after the pathologic report on the tissue removed had been made. Thus it seems safe to assume that in several instances at least the procedures were not as radically done as they might have been had the diagnosis been previously known or at least strongly suspected, and one is tempted to speculate, therefore, whether or not these surgical results could not be improved on. At any rate it would appear that more attempts to treat patients in the early stage (when there is reason to believe that the disease still remains localized to a single area or to not more than two associated and contiguous areas) by surgical means are worthy of trial.

A far greater problem than the choice of initial treatment for patients with incipient lymphosarcoma is the program to be followed in treating those in whom the disease has already become advanced, either because of its inherent fulminating character or because of neglect or unsuccessful initial treatment. Few of these patients can be expected to survive even five years, and practically all will eventually die of their disease or some complications attributable to it. It might be reiterated here that only four patients having three or more areas of involvement survived the minimum five year period. One of these was lost track of after seven years apparently free from disease, but the remaining three eventually died of it.

Desjardins in 1923 frankly stated that he questioned the efficacy of roentgen therapy in prolonging life. It is assumed that this excepts those cases in which life is immediately threatened by the occurrence of mediastinal compression, intestinal obstruction or some other acute complication.

Minot and Isaacs in 1926, reporting on lymphoblastoma, produced figures showing a slightly longer survival of treated as compared with untreated patients, 2.88 and 2.45 years respectively. They concluded that treatment was of some benefit in cases destined to experience an acute course but was probably without influence on disease of a more chronic nature.

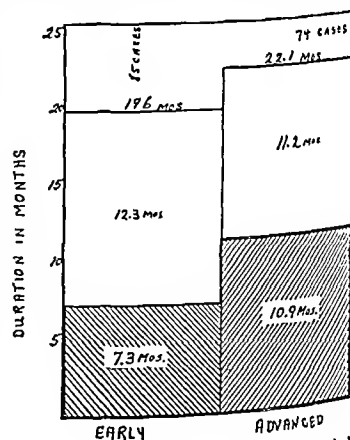


Fig. 11.—Relation of extent of clinical disease on admission to duration of life in patients dying of lymphosarcoma. The average duration of symptoms until initiation of treatment (shaded) was 8.7 months for all patients. The average duration of treatment until death (white) was 11.8 months for all patients. The average duration of the disease was 20.5 months.

Since all but two of the patients in the present series received some form of therapy, it was impossible to compare palliative results as measured by duration of life in treated and untreated groups. However, it seemed reasonable to suppose that some idea of its value might be obtained by comparing results for

TABLE 6.—Relationship of Type of Treatment to the Number of Patients Surviving Five Years or More

Type of Treatment	Total Cases	Indeterminate	Determinate	5 Year Cases	
				Survivals	Apparent Cures
X-rays alone.....	96 (49%)	36	60	9 (15.0%)	5 (8.3%)
X-rays plus radium..	26 (13.3%)	5	21	4 (19.0%)	3 (14.3%)
Radium alone.....	23 (11.7%)	6	17	0	..
Heublein alone or combined with radiation or surgery.....	22* (11.2%)	12	10	2 (20.0%)	0
Irradiation, all types.....	167 (85.2%)	59	108	15 (13.9%)	8 (7.4%)
Surgery alone or combined with radiation.....	30 (15.3%)	5	25	6 (24%)	6 (24%)
No treatment (far advanced disease).....	2 (1%)	..	2	0	..
Total.....	196 (100%)	64† (32.5%)	132 (67.5%)	21 (15.9%)	14 (10.6%)

* Three cases also included in the 30 cases treated surgically.
† Fifty-eight of these are patients admitted 1934-1935, now dead of disease.

patients appearing with incipient disease with results for those whose disease might be considered well advanced by the time treatment was sought. In selecting these two groups the extent of clinically demonstrable disease at the time of admission was used as the criterion, those presenting either a single involved area or two adjacent sites of disease being designated as "early" and all others as "advanced."

If treatment were of definite value in prolonging life one should logically expect that patients first seen with clinically early disease would have a much longer course than those whose treatment was instituted at a time when the disease appeared to be well under way. In other words, the survival of the early patients from beginning of treatment to death should be appreciably longer than that of the advanced patients. Actually there was very little difference (fig. 11), the early patients surviving 12.3 months and the advanced 11.2 months from the beginning of treatment. It was found, moreover, that the period of survival from onset of symptoms to application for treatment was 7.3 months in the early group as compared with 10.9 months in the advanced group. The total duration of the disease, therefore, from onset till death was 19.6 and 22.1 months respectively, a difference of 2.5 months (11 per cent) in favor of those whose disease was considered advanced on admission. It would seem, therefore, that the natural course of events had been either entirely unaffected or slightly hastened by treatment.

It might be recalled at this point that several forms of treatment and their combinations were employed and that the figures just cited represent a net average. A determination of the relative merits of each method consequently becomes imperative. This proved to be quite interesting (fig. 12).

Of all patients who eventually died of their disease, those treated with the element pack responded worst

and survived only 6.4 months from the beginning of treatment; those who received x-rays and radium reacted somewhat better and lived 9.6 months; those on whom x-rays (from 140 to 200 kilovolts) alone were employed lived 12.5 months; patients treated surgically with postoperative irradiation, usually x-rays, survived 12.3 months, and patients who received whole body irradiation (Heublein) supplementary to local irradiation lived 18.2 months from the time treatment was begun. This very orderly progression is difficult to explain but is so definite that it must be considered.

The group receiving a known amount of x-rays alone was the largest (seventy-nine patients) and could with some degree of accuracy be still further broken down. In addition, patients were included at least 75 per cent of whose treatment had consisted of this type of irradiation, forming a composite group of 114 cases. On subdividing these on the basis of size of the average treatment (fig. 13) it was found that patients receiving from 400 to 600 roentgens did best with a survival from start of treatment to death of 17.3 months as compared with 10.3 months for those receiving from 100 to 300 roentgens, 11.9 months for those given from 300 to 400 roentgens and 10.4 months for patients given average doses of from 600 to 800 roentgens. Thus it would appear that the small doses probably have too little killing effect on the disease, that the very large doses exert too marked an effect on the patient and that the intermediate doses probably bring about some compromise between the two. The average dose delivered per area also seemed to exert some influence on the duration of life (fig. 14). Patients receiving 1,000 roentgens or less per area survived only 11.6 months from the time of beginning treatment, whereas those receiving from 1,000 to 2,000 roentgens per area survived 14.1 months, those given from 2,000 to 3,000 roentgens 14.9 months, and those receiving 3,000 roentgens or more 13.1 months. It is naturally often impos-

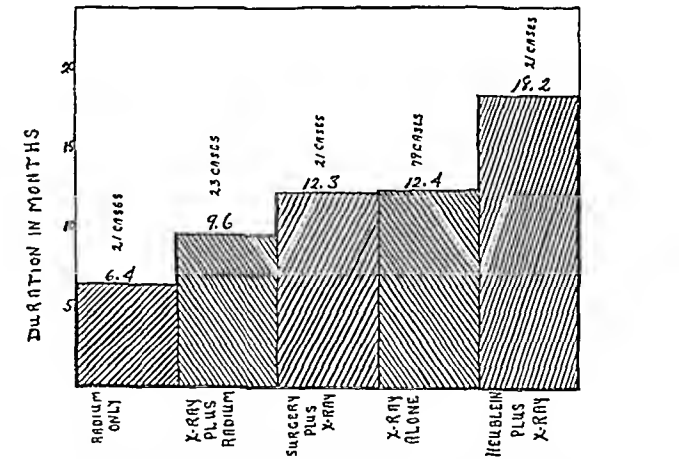


Fig. 12.—Relationship of type of treatment to the duration of life from the institution of treatment till death (average of all cases, 11.8 months).

sible to attain a dose of from 2,000 to 3,000 roentgens per area in patients with widely disseminated disease, but it would seem advisable to strive for this in those whose disease is apparently restricted to several areas and whose good state of general health will permit. Because prophylactic irradiation is in general not given at this hospital except as an adjunct to surgical therapy, the average treatment per course can merely reflect the inherent aggressiveness of the disease and adequacy

or inadequacy of previous treatment in controlling it. The former remains an unknown factor and the latter has already been presented.

SUMMARY AND CONCLUSIONS

The etiologic and clinical features and the results of treatment of 196 histologically proved cases of lymphosarcoma at the Memorial Hospital since 1918 were

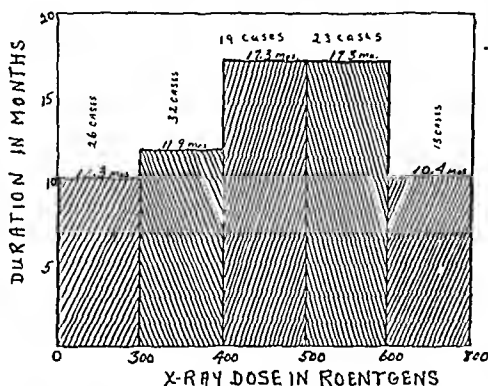


Fig. 13.—Relationship of the average dose per treatment to the duration of life in months (average of all cases, 11.8 months).

studied. Nine cases of giant follicular lymphoma were included, as that condition is here regarded as a type of lymphosarcoma. Hodgkin's sarcoma was excluded from this study.

The etiology of lymphosarcoma remains obscure. It is worthy of note that in 32 per cent of cases in which the first symptom was cervical lymphadenopathy there had been or was present definite chronic infection of the upper respiratory tract. The disease appeared to begin in the majority of instances as a local process and to spread mainly by cell emboli but perhaps also by the diffusion of some activating agent. It also seems possible that in some cases there were multiple foci of origin.

The age and sex distribution were as follows: Extremes of age were 4 and 88 years, with rather uniform distribution by decades, not more than 27 per cent of cases falling within any one decennium (from 50 to 59 years). The average age for both males and females was 45 years. The ratio of males to females was 7:3.

Reticulum cell lymphosarcoma was by far the most common type, accounting for 184 cases. Giant follicular lymphoma was diagnosed in nine cases. There were three cases of malignant lymphocytoma.

The early stages were characteristically free of constitutional symptoms and were signalized by the discovery solely of external lymph node enlargement in 65 per cent of cases. Abdominal symptoms were first noted in 17.5 per cent, upper respiratory tract symptoms in 11.6 per cent, thoracic symptoms in only 3.6 per cent and bone pain in 1.8 per cent.

As far as the records in this series show, lymphosarcoma most commonly begins and runs its early course only in lymph nodes. Two thirds of this series of patients never showed evidence of an extranodal primary lesion. In the one third in whom an extranodal primary lesion was found, it was located in one of the structures of the head and neck in 65 per cent, chiefly in the tonsil and nasopharynx. In 16 per cent the extranodal primary lesion appeared in the gastrointestinal tract, and in the remaining 19 per cent the primary lesions were miscellaneous and widely scattered.

The following were the sites of the first nodes found to be enlarged: neck 59 per cent, axillas 11.4 per cent, groins 11.9 per cent, abdomen 13.1 per cent, mediastinum 1.1 per cent and epitrochlear region 0.5 per cent. In 2.8 per cent (five cases) practically the entire node system appeared to be affected simultaneously.

According to the extent of the disease on admission, cases were classified as follows: (1) no evidence of disease (because of recent surgical removal) 3.6 per cent, (2) only one area affected 40.2 per cent, (3) two contiguous areas affected 12.5 per cent and (4) three or more areas affected 43.8 per cent.

Though early extension generally involves contiguous node groups, later involvement of distant organs is most reasonably explainable by the hematogenous route. The spleen was palpable in 21 per cent of cases (compared with 45 per cent in our Hodgkin's disease series). The liver was palpable in 8 per cent (Hodgkin's disease 24 per cent). Pleuropulmonary disease was shown roentgenographically in 12 per cent (Hodgkin's disease 29 per cent). Osseous lesions were found in 9 per cent (Hodgkin's disease 24 per cent). Metastatic skin lesions occurred in 5.5 per cent.

Anemia is in general slower in developing in lymphosarcoma than in Hodgkin's disease. There is no characteristic blood picture for lymphosarcoma. With the exception of 6.6 per cent of cases in which a more or less typical leukemic blood count was found, the differential count in general showed a predominance of cells of the granulocytic series.

The various methods of treatment employed included x-rays (from 140 to 200 kilovolts), radium (mainly the 4 Gm. element pack), x-rays and radium combined, Heublein total irradiation (usually combined with local external irradiation) and surgical extirpation (generally followed by local irradiation). So-called prophylactic irradiation was not carried out except as a supplement to initial surgical therapy.

Results of treatment were as follows: In a determinate group of 132 cases there was a five year survival rate of 15.9 per cent; 10.6 per cent of the patients are living after five years or more and are apparently cured.

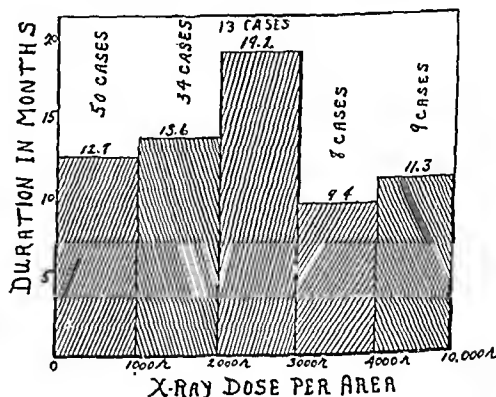


Fig. 14.—Survival from beginning of treatment till death as related to the average dose per area (average of all cases, 11.8 months).

Of the twenty-one patients showing a five year survival, only four had more than one area affected initially.

Among the factors influencing the course of the disease are (1) its individual inherent qualities for growth and dissemination, probably most important though least definable, (2) the extent of disease on admission, (3) location of the primary lesion, (4) complicating pseudo-leukemia or leukemia and (5) the age of the patient.

Analysis of the results of treatment suggests that (1) for clinically early (single area of involvement) and easily accessible disease radical surgical removal followed by prophylactic external irradiation is at least worthy of serious consideration and further trial and (2) for the more advanced stages of the disease either local roentgen irradiation plus total roentgen irradiation or local roentgen irradiation alone is superior to local roentgen plus radium pack irradiation or radium pack irradiation alone.

A study of roentgen dosage in relation to results suggests that divided dose therapy, using single doses in the order of from 400 to 600 roentgens and total doses per field in the order of from 2,000 to 3,000 roentgens, yielded the best results.

York Avenue at Sixty-Eighth Street.

EXTRAGENITAL TRANSMISSION OF SYPHILIS AMONG FIVE PER- SONS IN ONE FAMILY

A CASE REPORT

GRADIE R. ROWNTREE, M.D.

AND

JAMES ROBERT HENDON, M.D.

LOUISVILLE, KY.

Report of these five cases of syphilis is made because of many unusual features involved. Infections with *Spirochaeta pallida* due to husband-wife transfer are not uncommon nor is congenital syphilis by any means a rarity. There have been, however, no reports of multiple infections within one family identical with the study outlined here.

REPORT OF CASES

On Oct. 16, 1939, Mrs. E. X brought her daughter Paula, aged 18 months, to the surgical dispensary of the Louisville City Hospital because of a sore on the baby's lower lip. This had appeared from six to eight weeks previously. The child had been taken to a physician, who diagnosed the lesion as one of impetigo and prescribed an ointment. In spite of the use of this preparation the lesion had persisted and progressed, and approximately four weeks later the child's body had been covered with a reddish rash which faded after seventy-two hours.

At the initial examination of the patient in the surgery there was seen a pinkish discoloration of the lower lip on the right involving the mucous membrane and extending downward. This area measured 2.5 by 1.5 cm.; there was no discharge and no break in the continuity of the skin. Beneath the skin in this area was an indurated mass which was not tender. No additional lesions were seen within the mouth, although the tonsils were markedly hypertrophied. There was enlargement of the anterior cervical glands bilaterally, and there was generalized lymphatic enlargement of a lesser degree. A small crusted ulcer was present on the anterior skin fold of the left axilla. The observations were otherwise not remarkable.

Syphilis being suspected by the surgeon, the child was referred to the diagnostic clinic. Here a dark field examination of material from the axillary lesion was attempted but was unsuccessful. The blood Kahn reaction was strongly positive. The diagnosis was secondary syphilis with extragenital primary source.

An epidemiologic study of the entire X family, including a boarder in the home, was immediately made. This study included a careful history and physical and serologic examination of each member.

The following disclosures were made:

Mrs. E. X, the mother, was nonsyphilitic.

Mr. H. X, the father, was nonsyphilitic.

R. X, a son aged 15, was nonsyphilitic.

J. A. X, a son aged 8, was nonsyphilitic.

J. X, a son aged 4, was nonsyphilitic.

H. X, a boarder aged 23 and no relation, was nonsyphilitic.

Jess X, a daughter aged 11, had a discharging indurated nontender ulcer on her lower lip (fig. 1). This had appeared about three weeks previously (three weeks after appearance of the primary lesion on Paula's lip). Jess's anterior cervical glands were enlarged; others were not palpable. A dark field examination of material from the lesion on the lip was positive for *Spirochaeta pallida*. The diagnosis was primary syphilis.

Charles X, a son aged 6, had a fissured encrusted lesion between the pinna of the left ear and the head (fig. 2). There was general lymph gland enlargement, and the body was covered with ham-colored macules less than 1 cm. in diameter. A dark field examination of material from the ulcer was positive for *Spirochaeta pallida* and the blood Kahn reaction was strongly positive. The diagnosis was primary and secondary syphilis.

Valerie X, a daughter aged 17, had a superficial white excoriation about 5 mm. in diameter involving the mucous membrane inside the lower lip. There were two small vesicles on the external surface of the lip. The pharynx was inflamed; the tonsils had been extracted. The cervical glands were enlarged bilaterally. The blood Kahn test was strongly positive. There had been no history of any earlier lesions on the mucous membranes or on the skin. The diagnosis was secondary syphilis.

Two blood Kahn tests made on Clark X, a son aged 19, were strongly positive. He was unaware of any history of



Fig. 1.—Primary syphilitic lesion of lower lip of child aged 11.

a primary lesion or of secondary lesion but later recalled that he had had a severe sore throat in June or July 1939. The symptoms were described by him as being associated with yellowish blisters on the back of the tongue and on both tonsils. He was seen at that time by a physician, who pronounced the condition to be trench mouth and prescribed a gargle. After about ten days the subjective symptoms subsided. Immediately after this he noted that reddish areas of various sizes appeared on his face after shaving. These were hard to the touch, not tender and did not become pustular. They seemed to him to be

located under the skin. They were present for a few hours after shaving and then disappeared, to return the next time he shaved. After about two weeks they disappeared permanently. On examination a small ulcerated lesion was seen on the right tonsil and there was generalized lymphadenopathy. Results of the examination were otherwise not remarkable. A dark field examination was not made. The diagnosis was early latent syphilis.

Careful questioning of all members of the family except Clark revealed no outside contacts. Clark denied any sexual contacts for a year preceding his sore throat, but he recalled that in the winter of 1939 he had been on a "necking party" with Molly K., and a short time later had gone on a hay ride with Mary K. All other contacts were denied.

Molly K. was found to be nonsyphilitic. Mary K. could not be found. It was learned, however, that she had been admitted to the syphilis clinic of the Louisville City Hospital on Aug. 12, 1938, at which time a dark field examination of a lesion on her lower lip was positive for *Spirochaeta pallida*. She had received thereafter eight intravenous injections of an



Fig. 2.—Primary lesion of syphilis behind pinna of left ear of child aged 6.

arsenical and eight intramuscular injections of a bismuth preparation. On September 30 she had lapsed from treatment and all efforts to trace her had been unsuccessful.

To reconstruct the history of these cases, it is reasonably certain that Mary K. was the ultimate source of these five cases of syphilis. Through kissing she transmitted the disease to Clark X, who in fondling his baby sister passed the infection to her. Jess, Valerie and Charles X were infected by the same means. It is only fortunate that the entire family was not similarly stricken, since they are affectionate people and no precautionary measures were taken.

Of great interest is the fact that two syphilitic lesions were seen by a physician and diagnoses of relatively innocuous conditions were made. It is hoped that this report will serve to lower the threshold for suspicion of syphilis in the minds of practitioners and that thorough examinations will be made of all lesions which might possibly be syphilitic.

Clinical Notes, Suggestions and New Instruments

SULFATHIAZOLE: TWO CASES OF SEPTICEMIA WITH RECOVERY

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The sulfonamide group of drugs has opened up tremendous potentialities in the field of chemotherapeutics and many new avenues for the use of such drugs undoubtedly will be opened.

The limitations of sulfanilamide have been realized and it has become necessary to explore the field further to find synthesized derivatives of this drug which would act where the parent drug has failed, such as in instances of *Staphylococcus aureus*, *Streptococcus faecalis* and other resistant organisms. The introduction of sulfapyridine soon followed which seemed to offer potentialities that sulfanilamide did not possess. However, it exhibited serious side effects. Antopol¹ recently reported that 40 per cent of a group of patients receiving sulfapyridine showed hematuria. Pepper and his associates found this complication in twenty-seven of 381 patients taking sulfapyridine. The formation of urinary calculi has also been reported in many instances. Nausea and vomiting not infrequently interfere with the continued administration of this drug, and it is thought to be central in type rather than due to local irritation of the stomach.

Recently two thiazole derivatives of sulfanilamide have been placed before the profession for clinical investigation. These are sulfathiazole and its methyl derivative sulfamethylthiazole. The former is the thiazole analogue of sulfapyridine: 2-(para-aminobenzene sulfonamido) thiazole.

Long² has pointed out that the acute toxicity of sulfathiazole is definitely less than that found with sulfapyridine or sulfamethylthiazole. In experiments on rats and monkeys little evidence of injury to the body was found after these animals had been subjected to intense therapy with this drug. Van Dyke and his co-workers³ say that sulfathiazole disappears from the blood more rapidly than does sulfapyridine and is also excreted more rapidly. The proportion of conjugated sulfathiazole excreted in the urine was also less than was the case with sulfapyridine. Long confirmed these observations, using mice for his experimental studies. For hemolytic streptococcus and pneumococcus infections in animals, sulfathiazole was found to be slightly less effective than sulfapyridine when administered by mouth. For staphylococcal infections, however, it was found superior to sulfapyridine. Further studies have shown that it is more readily absorbed from the gastrointestinal tract than is sulfapyridine and is more rapidly excreted. Less of the sulfathiazole is acetylated or conjugated in the urine than is sulfapyridine, which would therefore allow more of the free drug for bacteriostasis than would the other substances.

Hill⁴ also points out that sulfathiazole is not as freely conjugated as are the other sulfamido products. White, in discussing Hill's paper, raises the question of whether sulfathiazole may undergo decomposition in the body with the excretion of a bactericidal cleavage product. Hill further states that the much larger amount of sulfathiazole which may be expected in urine as compared with sulfanilamide and sulfapyridine indicates the possibility that sulfathiazole may be a more valuable antiseptic than either sulfanilamide or sulfapyridine.

In the past, the prognosis in blood stream infections caused by the staphylococcus organism has been very poor. Kelliher⁵

Read before the Mid-Atlantic Branch, American Urological Association, Washington, D. C., April 6, 1940.

The assistance of the Department of Medical Research of the Winthrop Chemical Company made these studies possible.

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2. Long, P. H.: Thiazole Derivatives of Sulfanilamide, *J. A. M. A.* **114**: 870-871 (March 9) 1940.

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4. Hill, Justina H.: The Comparative Vitro-Action of Sulfanilamide, Sulfapyridine and Sulfathiazole in Urine, *J. Urol.* **43**: 491-495 (March) 1940.

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recently reported a case of septicemia with recovery, sulfamethylthiazole being used as the therapeutic agent. Pool and Cook⁶ report a series of cases in which sulfathiazole and sulfamethylthiazole were used and found that approximately 65 per cent of the patients were cured with this form of medication. In several of these cases the infection was caused by *Staphylococcus aureus* and *Streptococcus faecalis*. They found little evidence of toxicity from either drug. Other workers, however, report that sulfamethylthiazole has produced peripheral neuritis in some instances and seems more toxic than sulfathiazole. Herrell and Brown⁷ report a case of fulminating septicemia caused by *Staphylococcus aureus* in which sulfamethylthiazole was used with curative effects. Lindsay⁸ has used both of these sulfanilamide derivatives in a number of cases of systemic infections and has found that both drugs are very effective.

REPORT OF TWO CASES

In view of the small number of similar cases reported in the literature, it is thought worth while to report two cases of septicemia in which sulfathiazole was used effectively by me.

CASE 1.—H. B., a man aged 70, entered Garfield Hospital Feb. 24, 1940, and was seen in consultation with Dr. D. W. Prentiss. The patient was in a comatose condition, which had been present for twenty-four hours. The initial attack was ushered in by a chill, rigor and marked elevation of temperature. His wife stated that he had been disoriented for the past week, gradually becoming more stuporous as the illness had progressed. He had been nauseated and vomited a greenish, bile stained fluid. During the last twenty-four hours he had had marked diarrhea. The patient had been well for the past three or four years and had never had a previous similar attack. His past history was irrelevant.

The patient was senile and completely disoriented. He was quite toxic and dehydrated, and on admission to the hospital his temperature was 101.6 F., pulse rate 140 and respiratory rate 26. His tongue was covered with a foul whitish coating. Optic and other reflexes were sluggish and the patient did not respond to questions. The chest was normal aside from evidence of a low grade hypostatic congestion of the base of both lungs. The abdomen was distended similarly to the condition seen in paralytic ileus. No masses could be palpated and no evidence of tenderness was elicited. The genitalia were normal, as was the prostate on rectal examination. Examination of the rest of the body was negative. A hemogram showed 64 per cent hemoglobin, 3,300,000 red blood cells and 12,400 leukocytes. There were 70 per cent polymorphonuclears, 7 per cent band forms, 19 per cent lymphocytes and 1 per cent monocytes. A specimen of urine showed many clumps of pus, no red blood cells and no sugar. Culture yielded *Staphylococcus aureus*. A moderate trace of albumin was found. A few hyaline and granular casts were seen on microscopic examination.

Nonprotein nitrogen of the blood was 75 mg. per hundred cubic centimeters. A blood culture was made by Dr. Lindsay and yielded pure *Staphylococcus aureus*. After a consultation, an initial dose of 4 Gm. of sulfathiazole was given, followed by 1 Gm. of the drug every six hours. This medication was continued for four days. The patient's temperature had been forming a septic curve but became normal after he was on this therapy for three days. A second culture was made after five days which yielded negative results. During the interim he was given perfusions of 5 per cent dextrose in saline solution daily to insure an adequate intake of fluids. Several days after admission to the hospital he became rational, showed interest in his surroundings and requested food. The ileus rapidly disappeared and the vomiting, which had been persistent, ceased. A third blood culture was made five days after the preceding one and was also negative.

An intravenous pyelogram was then made and showed a calculous pyonephrosis of the right kidney. The left kidney contour, pelvis and excretion were normal. Because of the anemia, he was given two blood transfusions in divided doses,

which increased his red cell count to 4,350,000 and the hemoglobin content to 83 per cent.

On March 27 a right nephrectomy was carried out under spinal anesthesia and a functionless kidney was removed. Following this procedure the patient responded rapidly and is now convalescent. The sulfathiazole level of the blood was checked on alternate days during the administration of the drug and was found to average 5 mg. per hundred cubic centimeters of blood. The patient showed no evidence of toxicity until the end of the fifth day, when he became slightly nauseated and refused food. The drug was then discontinued and the nausea disappeared. His temperature has remained normal since that time.

The second case is that of a nonhemolytic streptococcus blood stream infection in which sulfathiazole quickly sterilized the blood stream.

CASE 2.—C. S. W., a man, seen on March 11, 1940, complained of severe pain over the kidney area, with nausea and vomiting. The attack was initiated by a chill followed by a sharp rise in temperature. The pain in the kidney area became more acute, requiring an opiate to relieve it. The patient had had a similar attack four weeks before while on a vacation in Florida and had been confined to his bed for two weeks. His symptoms at that time were very similar to the present ones and he was given sulfanilamide, which brought about a gradual remission of his pain and fever.

The blood culture was made by Dr. Lindsay and yielded a nonhemolytic streptococcus infection. Culture of the urine yielded the same organism, together with the colon bacillus. The hemogram showed 89 per cent hemoglobin with 8,000 leukocytes and 84 per cent neutrophils, of which 67 per cent were segmented, 15 per cent band forms, 1 per cent young forms and 1 per cent myelocytes. There were 13 per cent lymphocytes, 2 per cent large mononuclears and 1 per cent basophils. The thermal curve showed a variation of from 100.6 to 104.6 F. during the height of the attack.

The patient was placed on sulfathiazole therapy, being given an initial dose of 4 Gm., followed by 1 Gm. every six hours. Within twenty-four hours there was a marked remission of the fever and on the second day it became normal and has remained so since that time. The drug was discontinued after three days without evidence of toxicity. An intravenous pyelogram was made subsequent to this attack and showed evidence of a long standing pyelonephritis, the pelvis being very small. No structural defects were noted.

ADVANTAGES OF SULFATHIAZOLE OVER SULFAPYRIDINE

Sulfathiazole seems to be less toxic than sulfapyridine, as pointed out by Herrell, Brown and others. Less of this drug is conjugated in the body, which implies a higher concentration of the drug for bacteriostasis.

Sulfathiazole is more rapidly metabolized than its predecessor. Studies of blood level concentrations and urinary excretion indicate that sulfathiazole is more quickly eliminated and that less evidence of damage to the kidneys is found. Sulfathiazole seems to possess equal bactericidal properties with sulfapyridine in staphylococcic, gonococcic, pneumococcic and meningococcic infections.

DOSAGE

Because of its rapid elimination, the interval between doses should be decreased to permit a more constant blood level concentration. In severe fulminating infections an initial dose of 2 or 4 Gm. may be given. One Gm. of the drug is then given every four hours for four or five days. Determination of the blood level concentration of the drug should be made on alternate days. Frequent urinalyses as well as checks of the red blood and leukocyte count are imperative.

Owing to the rapid absorption and excretion of sulfathiazole, the drug may be administered for longer intervals to obviate the possibility of a relapse of the infection.

CONTRAINDICATIONS TO SULFATHIAZOLE

Sulfathiazole possesses the same inherent tendency of the sulfonamide group to depress the hemopoietic system. However, this side effect has not been seen in any of my cases and can be obviated by frequent hemograms.

6. Pool, T. L., and Cook, E. N.: Sulfathiazole and Sulfamethylthiazole in the Treatment of Infections of the Urinary Tract, *Proc. Staff Meet., Mayo Clin.* 15:113-116 (Feb. 21) 1940.

7. Herrell, W. E., and Brown, A. E.: The Clinical Use of Sulfamethylthiazole in Infections Caused by *Staphylococcus aureus*: Preliminary Report, *Proc. Staff Meet., Mayo Clin.* 14:753 (Nov. 29) 1939.

8. Lindsay, J. W.: Personal communication to the author, 1940.

COMMENT

I have used sulfathiazole in fifteen other cases presenting acute urinary infections, five of which were gonorrheal urethritis. In four of these cases the drug sterilized the urinary tract within five days. It is of interest to note that two of the patients had not responded to sulfanilamide therapy. The other ten patients had acute infections of the upper part of the urinary tract without evidence of obstruction. In every case the response to this form of therapy was immediate, and negative cultures were obtained in eight of the cases.

CONCLUSIONS

1. In seventeen cases of various types of urinary infections sulfathiazole was administered. Many of these patients had not responded to sulfanilamide therapy. In the two cases which are reported in detail, striking results were obtained in staphylococcal and streptococcal infections.

2. Sulfathiazole seems, in my opinion, to be less toxic and more effective than the other members of the sulfonamide group, nausea being the only side effect seen, and this quickly subsided when the drug was discontinued.

3. In staphylococcal and other sulfanilamide-resistant infections, sulfathiazole offers a new avenue of attack which in the few cases in which it has been used seems to justify the claims made for it.

4. Sulfathiazole is absorbed and eliminated more quickly than sulfapyridine, so that the concentration of the drug in the blood is more difficult to maintain at an even concentration. This difficulty is obviated by giving the drug more frequently and over a longer period of time.

NOTE.—Since this paper was written, ten other cases of infections of the urinary tract have been treated with sulfathiazole: five of prostatic obstruction, five of gonorrheal urethritis. All five of the patients with gonorrheal urethritis responded rapidly to this drug and marked improvement was noted in the others.

1621 Connecticut Avenue.

SYNDROME OF MAJOR MENSTRUAL MOLIMINA WITH HYPERMENORRHEA ALLEVIATED BY TESTOSTERONE PROPIONATE

ROBERT B. GREENBLATT, M.D., AUGUSTA, GA.

Minor menstrual molimina are accepted universally with resignation by women and as generally unworthy of consideration by the physician. Major menstrual molimina, however, may be so intense as to be manifest as unbearable premenstrual tension which endures from seven to fourteen days. The pent-up strain fortunately finds sudden release with the onset of flow. There remains, however, a group of patients who at first welcome and then dread the profuse and often protracted menstruation that follows. The tense, nerve-wrought and weary patient is further weakened by the loss of blood and finds herself cleft between Scylla and Charybdis. The syndrome of hypermenorrhea with its precursive major menstrual molimina is clear-cut and distressing enough to warrant recognition and consideration. The alleviation of this syndrome by testosterone propionate therapy is frequently so striking as to merit this report.

REPORT OF CASES

CASE 1.—A white woman aged 30, a tertipara, had been pregnant six times. The menstrual history revealed that onset occurred at 15 years of age; the cycle was irregular with intervals of two, five or seven months and was attended by severe dysmenorrhea. She had a toxemia of pregnancy in 1935. Several months after parturition the cycle regulated itself. In the past three years she presented herself at the University Hospital Outpatient Department on various occasions with premenstrual headaches, nervousness, low abdominal pain and general discomfort and at other times for dysmenorrhea and profuse menstruation. She gave a history of having had several curettages and transfusions for bouts of menorrhagia. In July 1938 curettage revealed a hyperestrogenic type of endometrium. The basal metabolism, dextrose tolerance test and

blood counts were within normal limits. During the later part of 1938 she received intramuscular injections of blood from lactating amenorrheic women,¹ which more or less controlled her bouts of menorrhagia of from fifteen to twenty days' duration and reduced them to a hypermenorrhea of from seven to ten days (chart 1). Although the cycle was regular, the flow remained profuse. The prodromal syndrome of headaches, lumpy and painful breasts, abdominal bloating, nervous tension and fatigue was very marked for two weeks prior to the onset of each period. This premenstrual tension was dramatically relieved by the onset of flow.

The suction curettage performed on Feb. 2, 1939, revealed a healthy secretory endometrium. For several months attempts were made at improving the patient's general health. She received iron medication, vitamin B₁₂, cod liver oil, sedatives and other remedies. The syndrome of hypermenorrhea and premenstrual tension persisted. In August 1939 she received 5 and 10 mg. of testosterone propionate during the latter part of the cycle. The improvement in menstrual molimina and bleeding was remarkable. The treatment was continued each month, the doses varying from 10 to 50 mg. a month. The improvement in the tension as well as the breast pains was noteworthy and was sustained after therapy was discontinued. When estrogenic therapy was substituted, the syndrome of intense irritability and premenstrual tension returned.

CASE 2.—A moderately obese white woman aged 34, a tertipara, gave a long history of hypermenorrhea. The cycle was regular, with profuse bleeding occurring for from seven to twelve days, necessitating from twelve to fifteen pads a day. Premenstrual tension, abdominal bloating, premenstrual edema, crying spells and fatigue were particularly marked in her case. Suction curettage performed in 1938 on two different occasions at the onset of menstruation revealed an excellent secretory type of endometrium. Intramuscular injections of blood from lactating amenorrheic women aided in shortening only slightly the duration of the menses but did not materially affect the profuseness of the flow. The patient could not tolerate thyroid therapy. Surprisingly enough, estrogenic therapy in very small doses improved her well-being. However, the flow was just as profuse as formerly; moreover, the premenstrual edema appeared to be more pronounced.

The administration of from 10 to 50 mg. of testosterone propionate sufficed to reduce the flow to normal (chart 2) with more or less concomitant abatement of the prodromal symptoms. The patient felt more relaxed and stronger. Abdominal bloating was greatly reduced, premenstrual edema seemed to be lessened and the patient did not weep as readily. No treatment was administered prior to her October menstrual period, and all the symptoms as well as the hypermenorrhea returned.

1. Greenblatt, R. B., and Torpin, Richard: Menometrorrhagia, J. M. A. Georgia 28: 342 (Aug.) 1939.

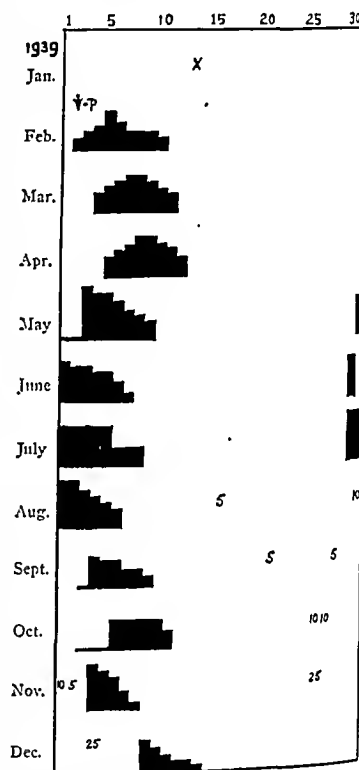


Chart 1 (case 1).—At x 25 cc. of blood from a lactating amenorrheic woman was administered. At the arrow suction curettage was performed, revealing an excellent progesterational type of endometrium. The numerals refer to milligrams of testosterone propionate.

However, treatment was omitted prior to her December period and the menses lasted but four days, with only two days of moderately profuse flow. The precursory symptoms seemed to be less severe than those she usually experienced prior to commencement of testosterone propionate therapy.

COMMENT

Frank² in 1931 reported fifteen cases of premenstrual tension and offered an acceptable explanation of the cause. Frank determined the levels of estrogen in the blood and urine of his patients and found a high renal threshold for the substance.

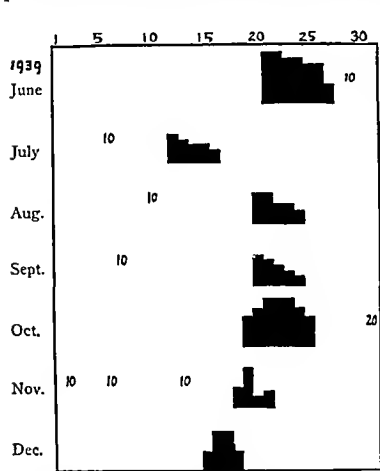


Chart 2 (case 2).—The numerals indicate milligrams of testosterone propionate. Suction curettage performed at the onset of menses on two previous occasions revealed good secretory endometrium. Note that no treatment was administered prior to the menses in October, with recurrence of the syndrome.

gested that premenstrual tension is caused not by an excess of circulatory estrogen but rather by the presence of unantagonized estrogen. By this he implied that the primary cause of premenstrual tension is deficient ovarian luteinization with a decreased production of progesterone. He therefore suggested progesterone therapy and/or low dose irradiation of the pituitary gland and ovaries. Among my records I found one report of a patient with marked premenstrual tension and dysmenorrhea who bled at irregular and lengthened intervals from a hyper-estrogenic endometrium. Cyclic administration of progesterone regulated her cycle and gave her complete relief.

The excellent progestational endometrium obtained at the onset of menstruation in my cases of cyclic hypermenorrhea with prodromal manifestations of major menstrual molimina precludes the complete acceptance of a hypothesis of corpus luteum deficiency. In another patient with this syndrome urinary pregnandiol glucuronide estimations were normal while urinary estrogens were insufficient for assay. I have noted among patients with varied degrees of menstrual molimina that estrogenic therapy frequently aggravated the prodromal symptoms and that when small doses of testosterone propionate were substituted the patient felt more relaxed. The employment of male sex hormone in the treatment of certain gynecic disorders⁴ may appear paradoxical but is not unphysiologic. Womack and Koch⁵ reported that normal women excreted quantities of androgens comparable to those excreted by normal males. The Callows⁶ isolated from the urine of normal women the same two androgens identified in the urine of normal males by

He therefore ascribed to premenstrual tension a hormonal pathogenesis. "It would appear," he wrote, "that the continued circulation of an excessive amount of female sex hormone in the blood may, in labile persons, produce serious symptoms, some cardiovascular, but most striking definitely psychic and nervous (autonomic)." At that time he suggested temporary or permanent amenorrhea, brought on by roentgen treatment, as the proper therapeutic procedure in severe cases.

Israel³ contested the explanation offered by Frank and sug-

Butenandt and his co-workers. The administration of chemically pure androgenic substances to relieve the syndrome of major menstrual molimina with hypermenorrhea seems indicated whether one accepts the explanation of hyperestrogenemia (Frank) or the concept of unantagonized estrogens (Israel). The indication finds further support in that male sex hormone nullifies and neutralizes the action of estrogens, for Shorr, Papanicolaou and Stimmel⁷ found that the follicular smear obtained with the injection of estradiol benzoate could be abolished by simultaneous injection of testosterone propionate.

CONCLUSION

The syndrome of major menstrual molimina associated with excessive cyclic bleeding is most harassing and distressing. Small doses of testosterone propionate were administered to two patients presenting such a syndrome with sufficiently good results to warrant its further trial.

A CONVENIENT METHOD OF APPLYING WET DRESSINGS

GAROLD V. STRYKER, M.D., AND JOSEPH GRINDON JR., M.D.
St. Louis

Various dermatoses affecting the hands and feet require the application of continuous wet dressings. The manner of application and the means of maintaining the moisture of such dressings present a practical problem. Sheets of wet proof material consume time to apply properly, are difficult to keep in place and are necessarily bulky.



Fig. 1.—Pliofilm mitt.

2. Frank, R. T.: The Hormonal Causes of Premenstrual Tension, *Arch. Neurol. & Psychiat.* 26: 1053 (Nov.) 1931.
3. Israel, S. L.: Premenstrual Tension, *J. A. M. A.* 110: 1721 (May 21) 1938.
4. Salmon, U. J.; Geist, S. H., and Walter, R. I.: Treatment of Dysmenorrhea with Testosterone Propionate, *Am. J. Obst. & Gynec.* 38: 264 (Aug.) 1939. Geist, S. H.; Salmon, U. J., and Gaines, J. A.: The Use of Testosterone Propionate in Functional Bleeding, *Endocrinology* 23: 784 (Dec.) 1938. Varangot, J.: L'action de la testosterone et de ses esters sur le tractus genital des femelles de mammiferes et de la femme, *Ann. d'endocrinol.* 1: 55 (March) 1939.
5. Womack, E. B., and Koch, F. C.: Testicular Hormone Content of Human Urine, *Endocrinology* 16: 273 (May-June) 1932.
6. Callow, Nancy H., and Callow, Robert K.: Isolation of Androsterone and Transdehydro-Androsterone from Urine of Normal Women, *Biochem. J.* 32: 1759 (Oct.) 1938.

These difficulties are overcome by the use of mitts and socks made of pliofilm.¹ This material is moisture proof, oil proof, odorless, nonirritating, pliable, thin, durable, tear resistant, sewable, heat sealing, not uncomfortably warm, noninflammable, resistant to weak acid and alkali and inexpensive.

7. Shorr, Ephraim; Papanicolaou, G. N., and Stimmel, B. F.: Neutralization of Ovarian Follicular Hormone in Women by Simultaneous Administration of Male Sex Hormone, *Proc. Soc. Exper. Biol. & Med.* 38: 759 (June) 1938.
From the Department of Dermatology, St. Louis University School of Medicine.

1. Pliofilm is made by the Goodyear Tire & Rubber Company, Inc.

Previously, one of us had employed rubber gloves and socks to maintain wet dressings over night. These were therapeutically effective, though patients objected because of constriction and excess heat.

Mitts and socks made of pliofilm have now been in use over a period of nine months, a total of eighty-seven private patients

having been so treated. In no case was there any evidence of irritation or serious complaint from the patient. In many instances the patient is grateful for the symptomatic relief obtained by the wet pack. By this method it has been possible to use continuous wet packs in cases in which before, owing to the inconvenience of application experienced, it would not have been feasible. In order to insure comfort, the coverings should be large enough to cover the dressings and at the same time permit some movement of the fingers and toes. To prevent drying, the pliofilm must come in contact with the skin of the wrist or ankle above the dressing.

In subacute and chronic phytosis of the hands and feet, borie

acid solution packs with pliofilm mitts and socks are used at night and a suitable antifungicidal ointment is applied during the day.

634 North Grand Avenue.

A MICRO BEDSIDE TEST FOR THE DETERMINATION OF THE SULFANILAMIDO GROUP CONCENTRATION IN BODY FLUIDS

E. W. SCHOEFFEL, PH.D., CHICAGO

The widespread therapeutic use of drugs containing the sulfanilamido grouping is safeguarded by methods which permit the constant observation of the effective concentration in the body fluids. However, the many untoward effects produced by these drugs force the physician to keep a close watch over his patients because of individual differences in toleration. (For toxic manifestations the blood picture is of major importance.) In the main, Marshall's¹ method is used. Several modifications of this test have recently been reported² which aim to simplify existing clinical laboratory procedures.

All known modifications were compared with one another. The following procedure was found to be simple, brief, feasible and economical. The method is reliable and reproducible in

the hands of student technicians. Since it is not necessary to report levels at all times in minute fractions but distinctions must be made between such concentrations as 3.5 and 4 or 2.5 and 3 mg. per hundred cubic centimeters of body fluids, this new modification is considered to rank with present procedures. Marshall's method together with the spot test filter paper method form the principal means by which this rapid test is accomplished. It is fitted for determination of the drug concentration in the blood, without the aid of laboratory facilities, by the physician or his technician at the bedside even in rural districts.

PROCEDURE FOR THE DETERMINATION OF THE SULFANILAMIDO DERIVATIVES BY THE MARSHALL SPOT TEST, FILTER PAPER METHOD

A. Place a drop of the body fluid under examination (approximately from 0.01 to 0.05 cc.) with calibrated pipets of the blood pipet type in the depression of a hanging drop slide. (The liquid may be dried by air current. If the material must be shipped, the dried substance is covered with a drop [from 0.050 to 0.075 cc.] of liquid petrolatum U. S. P. and the cover slip fastened on with a seal.) Place all slides on a clean white towel.

B. Add 0.02 cc. of four normal hydrochloric acid and 0.02 cc. of 10 per cent trichloroacetic acid to the material in the depression. Break up and stir thoroughly with a glass thread. For total sulfanilamide heat over an alcohol lamp to near dryness and repeat step B.

C. Add 0.03 cc. of 0.1 per cent sodium nitrite solution and stir the mixture thoroughly for thirty seconds (with amounts of free sulfanilamide in excess of 20 mg. for 100 cc. use 0.05 cc.) with a glass rod.

D. Add 0.02 cc. of a solution containing 0.1 per cent ammonium sulfamate and stir the solution thoroughly (for larger amounts of sodium nitrite use corresponding amounts of the sulfamate solution).

E. Add 0.02 cc. of 0.4 per cent aqueous solution of N(1-naphthyl)-ethylenediamine dihydrochloride (Marshall's reagent; the solution should be kept in a dark brown bottle and only enough made up to last two days). Stir the mixture thoroughly.

F. Prepare standards (as described under standard reagents and apparatus to be used for the test) containing 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12.5 and 15 mg. per hundred cubic centimeters. If testing for sulfanilamide, use sulfanilamide in the standards; if testing for sulfapyridine or sulfathiazole, use sulfapyridine or sulfathiazole standards, respectively. Such standards are good for one week if kept in an ice box and away from direct light. The standards may be conveniently prepared by carefully diluting a larger amount.

G. Insert in the depression containing the now red solution a strip of filter paper and let the liquid spread by capillary action over one end of the paper (precipitated protein material does not interfere with the test). Compare the unknown samples with the standards. The developed color depends on the drug used. (It is therefore necessary for the technician to know which of the sulfanilamido derivatives were used. It is important to know whether other therapeutic agents were also used. Especially with specimens of urine a slight color variation may be noticed, depending on various diazotizable substances. Since no fractions are to be determined and only round figures given [2.5, 4 and 7.5 mg. per hundred cubic centimeters], no strong interference exists.) The color on the filter paper will slowly fade but will hold distinctive and discernible hues for a period of days when compared with standards prepared on the same day and kept under the same conditions. Actual color charts may also be prepared to facilitate the determination at the bedside. In general for ease of reproduction the final amount of liquid in the depression should not exceed the approximate amounts of from 0.125 to 0.150 cc.

STANDARD REAGENTS AND APPARATUS TO BE USED FOR THE TEST

1. Standards containing drugs of the various sulfanilamido groupings in progressive proportions from 0.5 to 15 mg. per hundred cubic centimeters of liquid, depending on the accuracy desired. Amounts of 2.5, 5, 7.5, 10 and 15 mg. per hundred cubic centimeters are sufficient for reporting the concentration in body fluids. (The standard solutions should be made up to a p_H of 5 with trichloroacetic acid solution.)

Drs. W. C. Beck and H. J. Yellen, Cook County Hospital, gave permission to use samples of blood and of urine, and Dr. Howard Glass of the pharmacologic department of the University of Chicago compared the results of the Marshall procedure with those of the micro bedside method.

1. Bratton, A. C., and Marshall, E. K., Jr.: New Coupling Component for Sulfanilamide Determination, *J. Biol. Chem.* 128: 537-550 (May) 1939.

2. Ratish, H. D., and Bullowa, J. G. M.: A Bedside Test for Sulfapyridine, *J. Lab. & Clin. Med.* 25: 655 (March) 1940. Chinn, Herman, and Bellows, John: The Distribution of Sulfapyridine in the Body, *ibid.* 25: 735 (April) 1940. Demonstration before Cook County Hospital; personal communication to the author by the Chicago Branch Laboratory of the Illinois Department of Public Health. Vasterling, P.: The Influence of Sulfanilamido Derivatives on Urine Analysis, *Deutsche Apotheker-Zeitung* 55: 213 (April 6) 1940. James, G. V.: The Determination of Members of the Sulfanilamide Group of Drugs, *Analyst* 65: 206 (April) 1940.



Fig. 2.—Plioilm sock.

2. Hydrochloric acid, four normal.³
 3. Trichloroacetic acid, 10 per cent solution.
 4. Sodium nitrite, 0.1 per cent solution.
 5. Ammonium sulfamate, 0.1 per cent solution (containing 0.1 Gm. ammonium sulfamate per hundred cubic centimeters of distilled water).³
 6. Marshall's reagent, 0.4 per cent strength (containing 0.4 Gm. of N(1-naphthyl) ethylenediamine dihydrochloride in 100 cc. of distilled water).
 7. Filter paper (absorption strip paper for spot testing).⁴
 8. Hanging drop slides, cover slips and sealing material.
 9. Liquid petrolatum U. S. P.
 10. Glass threads.
 11. Suitable pipets (blood pipets or any other pipets standardized to require volume relationship).
 12. Equipment for obtaining blood from the finger or ear or for drawing spinal fluid.
 13. Alcohol lamp.
- 535 North Dearborn Street.

MYASTHENIA GRAVIS: TREATMENT BY IMPLANTATION OF DESOXYCORTICOSTERONE ACETATE PELLETS

ROBERT C. MOEHLIG, M.D., DETROIT

The more recent development of endocrine chemistry with the manufacture of synthetic, relatively insoluble, products bids fair to become an excellent way of treating chronic endocrine deficiencies. The advantages of this form of treatment are many and obvious.

I have recently treated a patient with a severe fulminating form of myasthenia gravis by the subcutaneous implantation of desoxycorticosterone acetate pellets.

REPORT OF CASE

M. G., a physician aged 32, complained Oct. 6, 1939, of severe dyspnea and rapid fatigability. The following is a report of his illness as written out by himself:

"The onset of the disease was insidious but rapid. There were no prodromal signs or symptoms of any infectious process.

"Dyspnea with the slightest exertion and fatigability with weakness were the major complaints. These were rapidly progressive over a period of seven days to the point of orthopnea and prostrating fatigue with but small effort. The patient could hardly raise his arms to shave or comb his hair.

"The weight of the head and shoulders and the effort to hold himself upright seemed intolerable and impossible. The muscles of the face, neck, shoulders, arms and chest were more involved than those of the abdomen and the lower extremities. The abdomen, however, became lax and protuberant, and defecation became more difficult.

"Impairment in swallowing foods or liquids progressed to inability to eat. Air was swallowed with all eating and drinking, producing excessive belching and gas pains.

"Paresis of the pharyngeal and laryngeal muscles produced a nasal, higher pitched voice, and talking was a decided effort, requiring frequent intervals of rest to avoid development of a whisper.

"Anorexia became complete in one week. All foods tasted alike. There was an 8.2 Kg. (18 pounds) weight loss within two weeks.

"The hard palate and nasopharynx were felt to be uncomfortably dry at all times.

"When the first symptoms of dyspnea and fatigue on exertion were noted, a generalized cold sweat would result from continued effort to be up and about . . . this, however, quickly changed to a dry skin with no sweating regardless of the amount of exertion.

"Orthopnea lasted for several nights and the weight of his arm on his chest wall could not be tolerated. The patient describes his dyspnea rather as an 'air hunger.' It was obvious

3. This may be omitted when rough approximations are being made.

4. This filter paper was obtained from Sargent & Co., Laboratory Supply House, Chicago.
Dr. Max Gilbert, of the Schering Corporation, supplied the desoxycorticosterone acetate material used.

From the Department of Internal Medicine, Harper Hospital and Wayne University College of Medicine.

to him that chest expansion and diaphragmatic excursion were diminished.

"Exertion always produced a bothersome tachycardia and palpitation, although no irregularity was noted.

"The patient had always been active and rarely took a nap or daily rest period. Shortly after onset, however, he felt utterly exhausted most of the time and was quite drowsy. He could readily fall asleep in a chair at any time of the day. Frequent short rest periods enabled him to continue with his work after treatment was started, although he never felt rested or strong, regardless of the sleep or rest he obtained.

"Sexual desire and powers were not affected. The sphincters were also normal."

The patient was tall and slender: 186.7 cm. (73½ inches) in height and 72.6 Kg. (170 pounds) in weight. He gave the appearance of being very ill.

He was extremely tired and exhausted. The expression of his face was apathetic and sad. The upper eyelids were ptotic and the forehead was wrinkled. Talking was obviously a great effort. He was able to say but a few words at a time and then had to wait a few minutes before resuming. He was incapable of any sustained muscular effort such as holding out his arms. His leg muscles tired easily when the leg was stretched out. Dyspnea was very obvious, and his respirations were about 30 a minute.

He had hyperextensibility of the joints, such as of the phalangeal and elbow joints.

The skin and mucous membrane of the mouth and of the pharynx were very dry. As he said, no matter how often he moistened his mouth with fluids his mouth would remain dry. Previously he had perspired profusely, especially in the axilla.

There was a tendency to external strabismus of the right eye. Nystagmus was not present. He had a high arched palate. The thyroid gland was palpable but not nodular. The heart and lung sounds were normal. There were no pathologic reflexes. Pes planus was present. The blood pressure was 110 systolic, 62 diastolic.

The serious condition of the patient called for immediate treatment, and urinary creatinine and other studies were not made.

The patient had three operations on his right eye for strabismus early in life. He had the usual childhood diseases.

The father is living and is a large, heavy set, muscular person, height 185 cm. (73 inches), weight 99.8 Kg. (220 pounds). The mother is living and is a heavy set woman, height 177.8 cm. (70 inches), weight 86.2 Kg. (190 pounds). A paternal uncle and a paternal aunt died of pulmonary tuberculosis. They were tall and slender. The patient is married and has one child.

October 7, treatment was begun as follows:

Quinine 0.6 Gm. three times a day, aminoacetic acid 4 Gm. three times a day and desoxycorticosterone acetate 5 mg. a day subcutaneously was the regimen. The quinine was discontinued after a few doses because of unpleasant effects.

As the first week passed under this therapy the patient's condition seemed to be about stationary. He was able to be up and about with difficulty. The aminoacetic acid was stopped after a few days. During the second week the injections of desoxycorticosterone acetate were increased to 10 mg. a day and definite, immediate alleviation of the fatigue and weakness was noted. This invariably occurred from five to six hours after the injection. The patient continued to improve slowly over the next ten days.

The daily injection of 10 mg. of desoxycorticosterone acetate was continued until October 28, when three pellets of 150 mg. each, or 450 mg., were implanted in the subcutaneous tissue of the left side of the abdomen.

Injections of the desoxycorticosterone acetate were stopped two days after the operative procedure. The patient's condition remained unchanged until the fifth day after the implantation, when he again rather suddenly noted another more marked alleviation of his symptoms.

Since then improvement has been gradual but steady, until at present, three and a half months after implantation of the pellets, no symptoms of the disease are noticeable. All loss of weight has been quickly regained.

As regards treatment, the patient's observation was that the quinine was of no apparent value. The aminoacetic acid was of very questionable value. The injections of desoxycorti-

costerone acetate were of definite though but temporary benefit, while the effect of the pellet implantations has been close to miraculous in its sustained and complete relief of symptoms.

Laboratory studies made Jan. 29, 1940, were as follows: blood sugar 70 mg., blood cholesterol 191 mg., nonprotein nitrogen 37.5 mg., blood creatinine 0.65 mg. (normal 1 to 2 mg. per hundred cubic centimeters of blood), urinary creatinine 13 mg. in twenty-four hour specimen of urine (normal 1 to 1.25 Gm. per twenty-four hour specimen) and blood chlorides 300 mg. of total chlorides as sodium chloride per hundred cubic centimeters of blood (normal from 570 to 620 mg. in 100 cc. of plasma).

It is unfortunate that comparative studies could not be made at the time the condition was at a crisis. It is of interest that the plasma chloride and blood sugar are lower than normal and are similar to the values seen in Addison's disease. This also holds for the nitrogen, which is somewhat higher than normal. Whether this means that the muscle was utilizing the creatinine after therapy rather than excreting it, as is usual in myasthenia gravis, is of course conjectural.

COMMENT

The diagnosis of myasthenia gravis was made on the basis of the history and objective manifestations. This was a very fulminating and severe type of the disease. The loss of weight was rapid owing to the patient's inability to eat properly, since solid foods would produce choking. The dyspnea was very marked, as was the muscular fatigue. His appearance was alarming.

The relief obtained by the injections of desoxycorticosterone acetate was definite and was more marked as the dosage was increased to 10 mg. a day. However, the most dramatic and striking improvement followed the implantation of the desoxycorticosterone acetate pellets. His improvement continued until February 20, 115 days after implantation, without a sign of recurrence and as late as June 7 he was still in good condition. He carries on his routine duties as a physician and is also able to carry on other activities such as dancing. He has regained the loss of weight so that he now weighs 80.7 Kg. (178 pounds). The dryness of the skin has also disappeared.

The rationale leading to the use of this synthetic adrenal cortical derivative was based on several factors. In a general way asthenia is an outstanding symptom of both Addison's disease and myasthenia gravis, although in the latter disease the fatigability comes only when the involved muscles are called on for sustained effort.

It was noted in the patient's past history that he had suffered from strabismus in infancy. This would indicate muscular weakness and, in view of the subsequent history, a congenital predisposition to muscle metabolism disturbance.

Both pituitary and adrenal cortex glands are concerned with muscle metabolism.

Houssay,¹ in his article on asthenia hypophysopriva, shows experimentally that the neuromuscular symptoms are due to alterations in the pituitary. He said "A neuromuscular syndrome appears in the hypophysectomized amphibians some weeks after operation and gradually becomes worse, terminating in death. Hypophysectomized toads (or toads from which the principal lobe has been removed) always become asthenic or adynamic at a later stage. Death occurs three to thirty days after the appearance of the asthenia, most of the toads dying between four and seven weeks after operation."

Pituitary insufficiency such as pituitary cachexia produces a very marked muscular asthenia comparable to that seen in Addison's disease.²

Houssay¹ found that the phosphocreatine (and also the total phosphorus) of the muscles was lowered after hypophysectomy. The muscular and hepatic glutathione diminishes. The resting muscular lactic acid is normal, but it increases less during tetanus than in the control patients.

In myasthenia gravis the excretion of creatinine is increased. Houssay said "Adrenal insufficiency, which occurs frequently in cases of pituitary insufficiency, probably increases the asthenia

but it is not certain, nor even likely, that the asthenia has an exclusively adrenal origin." Adrenal cortex extract "does not correct asthenia hypophysopriva as does the anterior pituitary extract. It is more probable that there is a direct metabolic action of the pituitary hormone. On the other hand the actions of the adrenals and pituitary on the carbohydrate metabolism have a certain similarity (the glycogenetic action, etc.) and anterior pituitary extract has a diabetogenic activity in adrenal-ectomized toads. Pituitary asthenia, therefore, appears to be due to general nutritive changes which principally affect the function of the central nervous system."

From the foregoing, a pituitary etiology of this condition seems not unlikely. If this is true, how does the synthetic adrenal cortical hormone produce its benefits? Probably by a secondary effect on the pituitary. Bates and I² showed that in an adrenal hypernephroma associated with polycythemia pituitary basophilism may be present. Furthermore primary adrenal cortex tumors which give a clinical picture simulating Cushing's pituitary basophilism no doubt activate the pituitary, even though a basophil adenoma is not present.

I have seen a few cases of pituitary dystrophy associated with progressive muscular atrophy and these patients, I believe, have a definite pituitary disturbance which is responsible for the muscular disease. Certainly the experimental work of Houssay would tend to strengthen this idea.

I have touched on some of these points in other articles, such as on the pituitary and adrenal cortex.³

It was noted by the patient that soon after the onset of the disease the skin became dry and there was no sweating, regardless of the amount of exertion. This is a symptom of pituitary insufficiency as emphasized by Houssay¹ and shown experimentally by his pupil Aubrun.⁴ Hypophysectomy in the toad produced cutaneous hyperkeratinization because of an exaggerated production and a failure of normal desquamation of the horny layers. The marked diminution of cutaneous secretions appears within from fifteen to twenty-five days after hypophysectomy. Injection of anterior pituitary extract restores the secretion of the skin.⁴

An inherited congenital muscular weakness in a person who is the offspring of hyperpituitary parents seems to me to be quite a logical hypothesis as the etiologic factor of myasthenia gravis; why, if this is correct, would the patient show what represents a hypopituitary disturbance?

It will be noted that a paternal uncle and aunt were asthenic and died of pulmonary tuberculosis. It is a well known fact that asthenic persons have, among other mesodermal weaknesses, poorly developed muscles and supportive structures.

Did this muscular weakness manifest itself congenitally in the patient as poorly developed musculature, as shown by the strabismus, hyperextensibility of the joints and pes planus?

Did this gland, when the patient reached the age of 32, produce a metabolic disorder in a congenitally weakened muscular system that manifested itself clinically as myasthenia gravis?

Schleizinger⁵ concluded from the results of therapy in seven cases of myasthenia gravis that anterior pituitary extract and aminoacetic acid are ineffective remedies. He found that the most satisfactory form of therapy in the absence of toxic manifestations consists in the oral administration of combined prostigmine and ephedrine medication.

Simon⁶ treated two cases of myasthenia gravis with anterior pituitary extract; the symptoms subsided with this form of therapy.

That the latter is a doubtful remedy, even if there is an involvement of the pituitary, is shown by the fact that solution of anterior pituitary in the form of "antuitrin" is not standardized and is of very questionable potency.

Prostigmine, as Schleizinger says, causes no permanent cure; "as with insulin in diabetes, continued administration is required. Progression of the disease may result in death despite the use

1. Houssay, B. A.: Functions of the Pituitary Gland, *New England J. Med.* 214: 913-926 (May 7), 961-971, 971-986 (May 14), 1023-1030 (May 21), 1086-1092 (May 28), 1128-1136, 1137-1146 (June 4) 1936.
2. Moehlig, R. C., and Bates, G. S.: Influence of the Pituitary Gland on Erythrocyte Formation, *Arch. Int. Med.* 51: 207-236 (Feb.) 1933.

3. Moehlig, R. C.: Pituitary Gland and Suprarenal Cortex, *Arch. Int. Med.* 44: 339-343 (Sept.) 1929; Selective Action of Suprarenal Cortex Secretion on Mesothelial Tissues, *Am. J. M. Sc.* 169: 553-564 (Oct.) 1924.

4. Aubrun, E. A.: Sintomas cutáneos de los sapos hipofisoprivos, *Rev. Soc. argent. de biol.* 11: 371-380 (Sept.) 1935; Síntomas cutáneos du crapaud hypophysoprivé, *Compt. rend. Soc. de biol. (Buenos Aires)* 120: 734, 1935.

5. Schleizinger, N. S.: Evaluation of Therapy in Myasthenia Gravis, *Arch. Int. Med.* 65: 60-77 (Jan.) 1940.

6. Simon, H. E.: Myasthenia Gravis, *J. A. M. A.* 104: 2065 (June 8) 1935.

of prostigmine. Certainly implantation of pellets of desoxycorticosterone acetate, if the remedy is efficacious, is a much more satisfactory mode of therapy.

Thorn and his associates⁷ found that the daily absorption of the pellets ranged from 0.25 to 0.3 mg. a day. Therefore on the basis of 0.3 mg. per pellet a day, roughly 1 mg. for the three pellets, the implanted supply would last approximately 450 days.

SUMMARY

Myasthenia gravis of the fulminating type with rapid loss of weight due to pharyngeal muscle weakness, dyspnea and muscular asthenia occurred in a physician aged 32; he was treated by hypodermic injections of synthetic adrenal cortical hormone (desoxycorticosterone acetate) and by implantation of three pellets (150 mg. each) into the subcutaneous tissue of the abdomen.

A pituitary etiology with a congenital inherited defect of the muscular system is postulated.

Improvement following the use of desoxycorticosterone acetate was both striking and dramatic.

While it is appreciated that remissions may and do occur in this disease, the patient's condition was precarious and the disease was rapidly progressive, so much so that death from respiratory muscular paralysis seemed imminent.

Naturally, further experiences with other patients as well as the continued progress of this patient is desirable before final conclusions concerning lasting benefits are made.

964 Fisher Building.

AN UNUSUAL CASE OF DUODENAL FOREIGN BODY

T. P. BROWN, M.D., AND ROBERT S. CREW, M.D.
PHILADELPHIA

E. W., a Negro woman aged 69, was admitted to the medical service of Dr. Russell S. Boles at the Philadelphia General Hospital, Aug. 15, 1939. Her chief complaint at that time was pain in the upper part of the abdomen. She had apparently been well until August 8, when she noticed a persistent dull pain in the right upper quadrant. She had been nauseated but had not vomited; the bowels had been regular; she had not observed any bloody, tarry or clay colored stools; her weight had been stationary.

Except for a cholecystectomy in 1931, her past medical and her family history were essentially negative. In 1933 and again in 1936 she had attacks of colicky pain in the right upper quadrant, which subsided promptly following medical treatment.

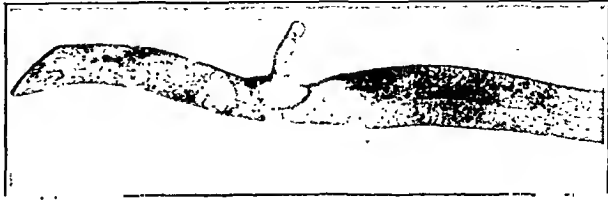
Physical examination showed no apparent abnormalities except an upper right rectus scar and a large firm irregular mass extending across the right upper quadrant of the abdomen, apparently attached to the liver. It was slightly tender on deep pressure and moved with respiration. At the time of examination a tentative diagnosis of metastatic carcinoma of the liver was made.

Laboratory studies showed nothing significant: The red blood cell count was 3,220,000, the hemoglobin content was 75 per cent, the white cell count was 12,000 and the differential count was normal. The blood urea nitrogen was 9 mg. per hundred cubic centimeters; blood sugar was 68 mg. The Wassermann reaction of the blood was negative. Gastric analysis showed an absence of free hydrochloric acid, low total acidity and an absence of lactic acid and occult blood.

August 17, a flat x-ray film of the abdomen was made and revealed that there was a drainage tube about 17 cm. long just to the right of the spine; the kidneys were well visualized and normal in size and position. The psoas line on the left was well outlined but on the right was obscured.

August 24, under cyclopropane and ether anesthesia, a laparotomy was performed by Dr. P. A. McCarthy. When the peritonum was opened the mass described was found to be omentum which was wrapped around the lower edge of the liver and was adherent to the gallbladder fossa. The gallbladder was absent and the common duct was slightly dilated

and tortuous. The tube reported by the roentgenologist was felt through the wall of the duodenum. The latter was opened and a large twisted horizontal bar of a T tube was removed. The vertical, or drainage, bar had been broken off and the part retained had migrated into the duodenum, where further migration had been interrupted by the angulation of the duodeno-jejunal junction. The duodenum was closed, the upper part of



Horizontal section of T drainage tube which had been inserted into the common bile duct and was found eight years later in the duodenum.

the abdomen explored and the abdominal wall closed. Convalescence was uneventful except for a stitch abscess. The patient was discharged symptom free September 13.

Her previous record showed that she had had a cholecystectomy performed in 1931 and had been discharged with a T tube in situ. At that time she was instructed to return to the surgical clinic for after-care but failed to do so and did not obtain other professional treatment.

COMMENT

This case is of interest in that (1) it illustrates that a sizable foreign body can remain in the duodenum for a long period without producing notable symptoms, (2) it shows that a relatively large foreign body placed in the common duct can migrate to the duodenum, and (3) it reemphasizes the necessity of strict follow-up supervision in this type of case.

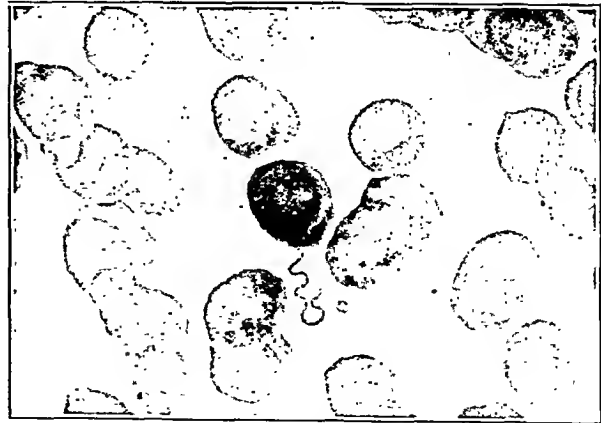
Philadelphia General Hospital.

REPORT OF A CASE OF RELAPSING FEVER

W. P. NEILSON, M.D., ENID, OKLA.

Relapsing fever, a disease found with relative frequency in certain tropical countries, has been rarely observed in the United States. For this reason, a typical case observed in a Midwestern state is of interest.

A woman aged 40 when seen on Dec. 19, 1939, had been ill for about six weeks. Her illness was characterized by recur-



Blood smear highly magnified.

rent attacks of elevations of temperature and repeated chills. She had been under medical treatment throughout this time, having been treated symptomatically, chiefly with large doses of quinine. There had been no improvement.

On routine examination I found that agglutination tests with antigens from tularcemia, typhoid and undulant fever were all

7. Thorn, George; Howard, R. P.; Emerson, Kendall, Jr., and Firor, W. M.: Treatment of Addison's Disease with Pellets of Crystalline Adrenal Cortical Hormone (Synthetic Desoxycorticosterone Acetate) Implanted Subcutaneously, Bull. Johns Hopkins Hosp. 64: 339-366 (May) 1939.

negative. There were no abnormal urinary changes. All physical examinations were negative. When I examined the blood smears I found many spiral organisms present. These spirochetes were unusually long, with seven or eight spirals. They were attached to the border of the red cells and extended well down into the intercellular spaces. I made a diagnosis of relapsing fever, although I had not previously seen a case. The laboratory examinations and the clinical picture made such a composite whole that I felt that the diagnosis was obvious.

On admission, the patient's temperature was 105.5 F. At 3 p. m. I gave her 0.4 Gm. of neoarsphenamine. At midnight her temperature was normal. Since that date there has been no further elevation. This is not surprising when it is realized that in the treatment of these cases in tropical countries one dose of 0.3 Gm. is curative in 80 per cent of the cases.

This case was reported to the Oklahoma State Health Department, with an inquiry about previous cases in the state. I was informed that no previous case has ever been reported in the state.

I am at a loss to know the origin of this infection; however, these facts are pertinent:

1. The patient has not been away from her immediate vicinity.
2. No foreign guest has visited the home.
3. There is no history of an insect bite or any other external lesion.
4. The patient lives on a farm in the wheat plains area; rodents are very few. She does no outside farm work.
5. I have been unable to find any more cases in this community.

The accompanying photomicrograph was made by the laboratories of the Oklahoma University Medical School.

502 West Randolph Street.

Special Article

CONFERENCES ON THERAPY

THE TREATMENT OF BLOOD DISORDERS

VII. LEUKEMIA, AGRANULOCYTOSIS AND NEUTROPENIA

NOTE.—These are actual reports, slightly edited, of conferences by the members of the Department of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital with the collaboration of other departments. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Treatment of Blood Disorders: VIII. Hemorrhagic Diseases."

DR. JACOB FURTH: Leukemia and agranulocytosis or neutropenia are two fundamentally different diseases, although the terminology would suggest that one is merely a depression, the other a stimulation, of leukopoietic activity.

Agranulocytosis or a milder form of it, neutropenia, can be produced by a variety of agents, and the process is reversible; that is, when the causative agent is removed complete restitution may occur. Leukemia, on the contrary, is a neoplastic disease of leukopoietic tissues, and removal of the causative agent after establishment of a neoplasm will no longer influence the course of the disease. This fundamental concept emphasizing the difference between these two types of disturbance is essential to the understanding of the established treatment of these diseases and to the evaluation of the new procedures that are proposed periodically.

In agranulocytosis, necropsy reveals either a hypoplasia of the granulocytic elements of the bone marrow or a normal number and occasionally an increased number of myeloblasts with failure of maturation. It is

assumed that at first maturation of the myeloblasts is arrested; and this is followed by an atrophy of the granulocytic elements of the bone marrow. We know of no agent that arrests maturation without producing subsequently a hypoplasia of the bone marrow. A maturation factor analogous to that influencing erythropoietic activity has thus far not been demonstrated in relation to the leukopoietic systems.

There are many agents which depress the granulocyte-forming elements of the bone marrow. These are: (a) chemicals, such as arsphenamine, benzene and related compounds, aminopyrine, dinitrophenol and more recently sulfanilamide and allied substances; (b) bacterial and protozoan products, e.g. those observed with streptococcal infections or kala-azar; (c) physical agents, as x-rays. Some of these agents act in almost every individual exposed, while others act only in a few of the individuals so exposed, who are assumed to be hypersusceptible to the specific agent. Cases in which the cause of agranulocytosis is not evident are spoken of as idiopathic, but there is no reason to believe that these forms of agranulocytosis differ in any way from those that are produced by known agents.

Leukocytes are constantly needed to ward off infections from micro-organisms that are normal inhabitants of mucous membranes. The chief danger in agranulocytosis is the absence of this normal protecting mechanism. Bacteria invade the mucous membranes, producing a necrotizing inflammation. Necrotizing angina can be both the result and the cause of agranulocytosis. In the *Index Medicus* agranulocytosis is listed only under "angina, agranulocytic." However, similar necrotizing inflammation with agranulocytosis may occur in places other than the oral cavity; it is not uncommon in the gastrointestinal tract. The goal of treatment is first to discover and remove the causative agent and then to stimulate granulocyte formation and maturation.

Leukemia is a neoplastic disease in which the malignant cells are primitive blood cells capable of unrestrained multiplication. The evidence in favor of this theory, reviewed elsewhere,¹ is overwhelming, and other views are not supported by sufficient evidence to merit consideration here.

Malignant blood cells may remain localized in one organ, producing a tumor infiltrating surrounding tissues. These forms of leukemia are spoken of as sarcomas, lymphosarcomas or myelosarcomas. More frequently the leukemic cells invade the blood stream, multiply by mitotic division and spread throughout the body, so that when the first symptoms appear the disease is widespread and appears to be systemic. Whether multicentric or unicentric at the start, in most instances leukemia appears to be systemic at the onset of the disease. The number of immature leukocytes in the circulating blood is, as a rule, of little significance. Interference with the function of organs which are infiltrated is the chief difficulty in leukemia. Irrespective of the primary site, all malignant blood cells have an affinity for the bone marrow, where they crowd out the other elements or otherwise interfere with the formation of normal granulocytes, erythrocytes and thrombocytes. Since leukemic cells themselves function as normal blood cells to only a limited degree, leukemia itself may be the indirect cause of an agranulocytic type of inflammation. The function of other infiltrated organs is similarly interfered with. The

1. Meulengracht, E., and others: Symposium on the Blood and Blood-Forming Organs, University of Wisconsin Press, 1939.

sites of infiltration vary considerably with different cases. The primary symptoms are referred to the bone marrow, brain, spleen, kidney or almost any other organ.

The causes of leukemia are unknown. Experimental studies in animals indicate that both intrinsic, that is hereditary, and extrinsic, or environmental, factors are responsible for it. The leukemias observed in man are of unknown etiology, with rare exceptions, e.g. cases occurring in persons exposed to x-rays or benzene. Neoplastic cells are not controlled by removal of the agent which has produced them; a knowledge of the etiology of leukemias might help in preventing the disease but promises little as regards treatment.

Leukemic cells, like neoplastic cells in general, are slightly more vulnerable to physical and chemical agents which injure normal blood cells; hence the decrease of the number of leukemic cells by properly adjusted doses in any part of the body is a feasible procedure. About this Dr. Forkner will speak to you.

TREATMENT OF LEUKEMIA

DR. ADE T. MILHORAT: Dr. Forkner will discuss the clinical aspects of the subject.

DR. CLAUDE E. FORKNER: One may adopt a more optimistic attitude in regard to the therapy of leukemia than is indicated by the term neoplasm, for it appears that in some cases of leukemia, at least, the process is reversible. The occurrence of spontaneous remissions in leukemia is an illustration. In these a full-blown picture of leukemia proved in biopsies of the bone marrow regresses until both the blood and the bone marrow structures return to normal. A few months later the condition recurs and the patient dies of it. The fact, however, that there is this reversibility introduces a hopeful element for the development of effective therapy.

Although leukemia is a fatal disease, much can be done about alleviating the symptoms and making the patients more comfortable. That applies especially to the chronic forms. Among the general measures which may be used to alleviate the symptoms are rest and regulation of activities. Patients with leukemia complain often of weakness. They may complain of feeling excessively tired. These frequently are manifestations either of the increased basal metabolic rate or of anemia. There may be symptoms referable to pressure of some enlarged organ on other important organs. Patients with leukemia should be guided in their activities, depending on their general physical state, their activities being limited to avoid undue fatigue and when they are in a state of remission again their activities being increased. One should not regard the leukemic patient as an invalid. Frequently I see patients with a diagnosis of chronic myelogenous leukemia or chronic lymphogenous leukemia whom the physician advises to stay in bed and to restrict their activities markedly. Even though they have some symptoms, rigid restriction of activities is undesirable. I think a patient with leukemia should be allowed activity compatible with his general state, with the anemia, with the symptoms of increased metabolism and with the enlargement of the spleen or liver. Often a patient with chronic leukemia can play golf, swim and engage in other activities almost to the extent of a perfectly well person.

One often is asked about food for patients with leukemia. Should they receive a special diet? This is not of particular value in leukemia. A number of my patients with chronic myelogenous leukemia, particu-

larly the more intelligent ones, have themselves found that they feel better if they take large quantities of fats. Some patients have said that unless they have generous amounts of butter or cream they do not feel well. One patient said that she eats three times as much butter as any other member of the family, and if she does not eat butter she cannot do her work. The explanation may be that these patients have a high basal metabolic rate and that fats are a good source of energy. Also it is sometimes important to feed patients with leukemia at frequent intervals. Instead of three large meals they may perhaps have five or six small meals, the reason being that the spleen and the liver are at times so greatly enlarged that they encroach on the organs of digestion so that patients cannot fill up their stomachs without discomfort. In general, the diet of the patient with leukemia should be well balanced, as high in calories as the patient can tolerate and should have an adequate quantity of accessory food substances.

Frequently one is asked Should a patient with leukemia seek a more equitable climate? Should he go to Florida or to California? There is no evidence to suggest that climate has anything to do with leukemia, but it is advisable of course as far as possible to avoid respiratory infections. Perhaps under certain circumstances, particularly if the patient is subject to respiratory infections or sinus disease, he may do better in a climate where the weather does not change rapidly. Oral hygiene is also important in the treatment of leukemia. These patients are susceptible to infections about the teeth and the mucous membranes. This is particularly true in the later stages of chronic leukemia and in acute leukemia. One must be careful to have them cleanse their mouths gently. Conservative means should be employed in the treatment of any lesions of the mucous membranes, of the teeth or of the mouth. Frequently patients have toothache, and they go to their dentists before they go to their physicians. As you know, these patients have a special tendency to bleed; they may become almost exsanguinated as a result of a simple tooth extraction. Any operative procedures that are necessary should be carried out under careful supervision, preferably in the hospital, and if there is bleeding from the nose or from other mucous membranes only conservative measures should be taken. Transfusions of blood may be of value. Cauterization of bleeding areas should be done with great reluctance.

In a previous conference we covered the subject of the roentgen treatment of diseases of the blood; in that conference we discussed the treatment of leukemia in detail and we said something about the selection of cases for treatment. I want to repeat just two or three of those matters briefly: First, the fact that a patient has leukemia is not sufficient reason for immediate treatment with x-rays or with any other procedure. The treatment is essentially symptomatic. We cannot cure the disease by x-rays, benzene, arsenic or any other procedure. We treat patients in order to relieve their symptoms, and subsequently we try to anticipate the next relapse, treating them if we can before a relapse occurs. By careful observation of the blood, the basal metabolic rate and the patient's physical condition, we can often anticipate the onset of another relapse and forestall it by giving treatment before it actually occurs.

Patients with acute leukemia do not respond to any form of treatment as a rule; occasionally some improve-

ment is obtained, but it is evanescent and usually disappears in the course of a few days. Why some of these patients rarely have spontaneous remissions no one knows. All patients with chronic leukemia eventually come to a refractory state where no treatment is effective; where the cells in the bone marrow, in the blood and in the lymph nodes for some reason or other do not respond to roentgen treatment or to any other treatment. The treatment may decrease the number of cells but the patient may not be clinically benefited.

Although we treat patients with chronic leukemia fairly effectively with x-rays, radium, benzene and arsenic, these agents also are known to render individuals more susceptible to leukemia. This paradox may help one to understand why such agents fail to cure the disease.

Arsenic enjoys the reputation of being both the oldest and also the newest form of effective treatment of leukemia. Lissauer in 1865 first discovered that solution of potassium arsenite (Fowler's solution), which represents 1 per cent arsenic trioxide, was effective in reducing the leukocyte count and producing clinical betterment in patients with chronic leukemia. Cutler and Bradford at the Boston City Hospital in 1878 further studied the effects of this drug. They reduced the leukocyte count of a patient with chronic myelogenous leukemia from over a million cells down to 8,000 and produced dramatic betterment. When x-rays were found to be effective by Senn and others in 1903, the effects of arsenic were largely lost sight of because it was thought that x-rays actually constituted a cure for the disease. The opinion also developed that arsenic either had no effect at all in leukemia or that if it did have an effect it acted merely as a "tonic" and was beneficial in the anemia; but a great many workers felt that it had no specific effect on the leukemia. We have studied the effects of arsenic, particularly solution of potassium arsenite, and demonstrated rather conclusively that benefits accrue from treatment which are comparable to those of treatment with radium or with x-rays. A count can be brought from several hundred thousand per cubic millimeter down to normal. The anemia may completely subside. The basal metabolic rate can be reduced from +40 or 50 to normal. The bone marrow can be reversed from a frankly leukemic state to marrow that can hardly be recognized as leukemic. The patient will gain weight and feel much better. The spleen and the liver, which may be many centimeters below the costal margins, can be reduced so that they are no longer palpable. All signs of remission are induced, and such effects occur regularly in patients with chronic myelogenous leukemia. The drug is not so effective in chronic lymphogenous leukemia, but neither are x-rays so effective in that form of the disease.

The method of giving solution of potassium arsenite is to begin with small doses. We usually begin with 0.2 or 0.3 cc. (about 3 or 4 minims) of the solution three times daily after meals, well diluted in some food substance like coffee or orange juice, in order to mask the drug. It must be taken immediately after meals and regularly; if doses are missed frequently, the effects are not satisfactory. The doses are then gradually increased by about 1 minim a day until 8, 10 or even 15 minims (0.5, 0.6 or 0.9 cc.) three times a day is given. The exact amount varies with different patients. Along about the tenth or twelfth day the leukocyte count begins to drop precipitously. Within a few days the patient begins to feel better, the anemia is lessened, and all the symptoms of remission become apparent.

As soon as the leukocyte count reaches normal or near normal, the dose is gradually decreased by about the same rate of 1 minim (0.06 cc.) a day until the patient is taking 4 or 5 minims three times a day, and with that dose he can be maintained for many months, during which remission will persist. On the other hand, if the drug is discontinued abruptly, about three weeks later the leukocyte count will begin to rise and the patient will have another relapse. It is important to decrease the drug slowly just as it is to increase it slowly. We do not know exactly the reason for this, but it is an old observation which is borne out by recent studies. Minor manifestations of arsenic poisoning such as loss of appetite, slight diarrhea, perhaps slight nausea, chemosis of the conjunctiva and scaling and drying of the skin may be disregarded. More serious symptoms, such as peripheral neuritis, are rarely encountered, but when they are the drug must be discontinued.

Almost every clinic in the United States has discontinued the use of benzene in the treatment of leukemia, but I believe that this has been done without sufficient reason. I have seen a number of patients who have been successfully treated with benzene in doses of about 4 Gm. administered in capsules with olive oil by mouth daily. The evidence which has been presented against it, if reviewed critically, is found inadequate. The drug can be used effectively, but it must be used carefully. Recent studies by Kalapos, in which he has observed a large number of cases, indicate that the drug is worthy of use in leukemia.

AGRANULOCYTOSIS AND LEUKOPENIA

I do not think that agranulocytosis is merely an exaggerated form of leukopenia. I regard it as quite a different process. Acute agranulocytosis is something which comes on suddenly. It may appear on the basis of leukopenia or it may come on in a patient who has leukocytosis or leukemia. It is an acute episode with a definite syndrome, which then either goes on to death in about 70 per cent of the cases or to spontaneous or possibly induced recovery in 30 per cent of the cases.

Several measures have been advocated for its treatment. Friedemann as long ago as 1927 recommended roentgen treatment with small doses, one twentieth of an erythema dose, applied over the long bones, scapulas, sternum and pelvis, and claimed remissions in some cases. His group of cases was well selected and he tended to eliminate patients who had not been benefited within the first three days of treatment. Others have been unable to induce satisfactory remissions with this method. I do not think there is any good evidence that roentgen treatment, even though it is regarded as a stimulating dose, is of any value in the treatment of agranulocytosis. Frequently patients receive transfusions of blood, as it is thought that transfusions might supply leukocytes. Our own studies in agranulocytosis have shown that transfusions are of no value. In fact, in frequent counts of the blood we found that the white blood cell count was as a rule lower within two or three hours after the transfusions than it was before and that the leukocytes which are transfused disappear from the blood in the course of an hour or two. The studies which have been made of groups of cases, I think, do not demonstrate that transfusions are of any value in acute agranulocytosis. Dr. Reznikoff reported fifteen cases in which adenine sulfate was administered and he is going to say something about that later. Jackson, Parker and Taylor in 1932 suggested that pentnucleotide be given intramuscularly in daily doses of from 20 to 40 cc. in cases of agranulocytic angina,

on the basis of the theory that pentnucleotide or other nucleic acid derivatives might be effective in stimulating the bone marrow. Jackson's cases, again, were somewhat of a selected group, and I think that most clinicians feel now that perhaps the treatment with pentnucleotide is not as satisfactory as it was once thought to be. In his group 33 per cent of the patients died.

Liver extract has been given and thought to be effective, but there has not been any large series of cases in which the effectiveness has been proved. As a matter of fact there has been no satisfactory study of a treated group of cases of agranulocytic angina and a control group comparable as to age, nutrition, general state of health and blood picture in which any therapeutic agent has been shown to be beneficial. The most important factor in the treatment is, as Dr. Furth suggested, to remove the offending agent, if it can be found.

DR. MILHORAT: Would Dr. Reznikoff care to make a few remarks on agranulocytosis?

DR. PAUL REZNIKOFF: The term we prefer to use for this condition is not agranulocytosis. Although that is the most commonly accepted term, the better term I think is neutropenia or granulocytopenia because the neutrophils are the particular cells that interest us. Four factors have been considered instrumental in causing neutropenia. Dr. Furth has mentioned the first, namely certain drugs. I believe he omitted gold salts. A monograph written by Plum gives an account of the various drugs which tend to depress the bone marrow. Some workers believe that other factors are necessary. The patient must be susceptible before the drug can exert its effect. Other factors incriminated are undue fatigue, menstruation and possibly infection. In ordinary infections neutropenia is rare. Infections more commonly cause leukopenia but rarely neutropenia. Even though the total white blood cell count is very low, an adequate number of neutrophils is present in ordinary infectious leukopenia. In the typical attack of granulocytopenia, the decrease in the neutrophils precedes other phenomena. Kracke has demonstrated that the so-called agranulocytosis occurs before the angina.

As Dr. Forkner has indicated, prophylaxis is the most important aspect of the treatment of this condition. He has mentioned various agents that have been used. Watkins maintains that he has obtained good results with yellow bone marrow supplied by Armour. He gives it in doses of from 0.5 to 1 cc. I have given as much as 4 cc. of this oily extract by mouth three times a day, usually floated on some chilled tomato juice. Roentgen treatment is, I believe, dangerous, for while there is some apparent stimulation of the bone marrow due to transitory hyperemia, many of these patients show even more depression of the marrow after roentgen therapy than before. Liver extract has been given in doses similar to those used in the treatment of pernicious anemia, from 15 to 45 units a day intramuscularly, on the supposition that it might prove effective because in pernicious anemia the increase of the reticulocytes is accompanied by an increase of the white blood cells and polymorphonuclear cells. I believe that these two diseases are entirely different, however, and no good evidence exists that liver extract is effective. I agree with Dr. Forkner that transfusions are of no particular value, although they probably do no harm.

With regard to the nucleic acid derivatives, adenine sulfate is given intravenously in doses of 1 Gm. dissolved in about 25 or 30 cc. of hot saline solution

three times a day for about three days. The compound is insoluble except in hot solutions, so we dissolve the 1 Gm. in boiling saline solution and give it as warm as the patient can endure, being careful that none of it gets into the tissues outside the vein, where it will cause necrosis.

Pentnucleotide is given intramuscularly. Occasionally it produces severe reactions. I give it in small doses of 1 cc. at first; if it produces no untoward effects, the doses are doubled until 10 cc. is given four times a day. About all of these agents one may say that they are not specific, nor is there any good evidence, in my opinion, that patients have ever recovered through their use. A good example of how difficult it is to evaluate treatment of this disease is the experience of Dr. Dameshek of Boston, who once told me that he had never lost a patient to whom he gave adenine sulfate and believed that my claims concerning this compound were too conservative. Six months later he told me that he had had twelve patients who died after it was used.

In the prophylaxis of this disease one should refrain from the use of those agents known to cause it. Aminopyrine can perhaps be dispensed with, without great loss to the patient, although some appear to be unable to obtain relief from menstrual pain or headaches with other drugs. Sulfapyridine and sulfanilamide are also included among the chemical agents which cause this disease. It would indeed be a great misfortune to attempt to dispense with these. However, their dangers would be greatly reduced if physicians were generally made aware of the possibilities of neutropenia and used them only where there is definite indication and in those cases in which the possibility of their proving effective is fairly strong.

DR. MILHORAT: Dr. Craver of the Memorial Hospital has been able to attend this conference.

DR. LLOYD F. CRAVER: In myelogenous leukemia one of the difficult problems is the case in which the spleen has been reduced by irradiation and, while it is still small, evidence of relapse appears in the blood count. What is one to do next? Should one irradiate the spleen, which is still small, or should one irradiate the bone marrow or large sections of the body or even the entire body? We do not follow any fixed rule. In some cases we have irradiated the small spleen again; in others we have irradiated the bones, although in general we are fearful of very much irradiation over the bones, and in other cases we have tried general irradiation or large sectional irradiation.

We have not used arsenic much, especially in recent years, and I wanted to ask Dr. Forkner what routine, if any, he has with regard to the administration of arsenic in relation to cycles of irradiation. Does he use it concomitantly with the irradiation or only in the intervals between cycles of treatment, or does he restrict the treatment of selected cases to arsenic or to irradiation?

I would like also to put in my word along with Dr. Forkner's about the idea of leukemia being a neoplasm. I cannot speak, of course, from the pathologist's point of view or from the point of view of one who has experimented with animals. I can speak only from the point of view of the clinician who has seen a good many of these cases. My impression about leukemia is very similar to my impression about Hodgkin's disease, namely that it begins as an inflammatory process or an overresponse to something or other on the part of the organism. In the beginning I feel that it is probably not a neoplasm. I think of those acute

cases that Dr. Forkner mentioned and I am inclined to think that in some instances it may be a reversible reaction; but then in many cases it does go on in later stages to what is probably a neoplastic process, just as in the case of Hodgkin's sarcoma. I even think of lymphosarcoma in the same way, and undoubtedly lymphosarcoma is commonly thought of as a malignant tumor; yet as a large number of those cases are seen certain cases are encountered in which it begins as an atypical low grade process hardly distinguishable from an inflammatory process. I wonder if this is not simply a short stage of passage between an inflammatory process and a true neoplasm. I think the same remarks can be applied to many forms of neoplasms, such as epidermoid carcinomas, which appear to begin as some sort of tissue reaction which goes over into a true neoplasm.

DR. FORKNER: We would do as Dr. Craver has done, namely individualize patients. If a long time has elapsed since the patient has had any irradiation and if enlargement of the spleen and changes in the blood are associated with increasing anemia, with an increased metabolic rate or with distress of any sort, I think that the thing to do is to go ahead and treat that patient again. Give him just enough roentgen therapy to produce a remission. I do not believe there is any evidence to indicate that large doses of x-rays frequently repeated are of any more value in leukemia than just enough treatment to control the disease.

DR. CRAVER: Where would you apply the treatment in such a case?

DR. FORKNER: I feel as you do about treating the bones of a patient with leukemia. I think that the anemia is less likely to be relieved promptly and that one is more likely to get serious thrombocytopenia than if one treats other structures such as the spleen or thorax.

The total irradiation I myself have had relatively little experience with, but I feel somewhat afraid of total irradiation of the body in leukemia. We have seen a few bad results in which even after very small doses, as little as 35 or 50 roentgens applied to the front or back of the body, there have been a very marked drop of leukocytes, severe thrombocytopenia and persistent anemia. I think one can control the treatment better by limiting it to some particular part of the body. I should like to know what your experience has been with regard to total irradiation in cases of chronic leukemia.

With regard to the question of arsenic plus irradiation or arsenic alone or irradiation alone, I think that most patients with chronic myelogenous leukemia will have a thoroughly satisfactory response with arsenic and that it is easier to control the treatment with arsenic than with x-rays. As a rule, the drug therapy is less expensive than roentgen treatment. The treatment can be given in places where there is no access to radiotherapy machines. I think that frequently therapeutic methods can be alternated with profit, arsenic being given at one time and radiation at another. Arendt and Gloor in their series of cases reported in 1932 used that sort of treatment, giving arsenic plus radiation and arsenic alternated with radiation. They thought that they had better results and that they had actually prolonged the lives of the patients more by that means than they had by either agent alone.

DR. CRAVER: Total irradiation was first proposed between 1905 and 1907 in Germany by Dessauer

and a collaborator, but I do not believe they put it into practical use. It was not until after the war that some European workers began to irradiate the whole body of a patient for various radiosensitive processes, particularly the lymphoid diseases, leukemia and so on. The method has been mostly that known as the spray therapy. One simply backs off an x-ray tube to a sufficient distance, a meter or a meter and a half, so that its rays can encompass all or nearly all of the body. Our experience at the Memorial Hospital has been limited almost entirely to the Heublein method. We have a special unit consisting of two rooms with the x-ray tube mounted in the ceiling or between the rooms. The patients stay there in bed day and night and are exposed to radiation of a very low intensity, about 1 roentgen per hour, or now $1\frac{1}{2}$ roentgens, although I think that perhaps is a little too rapid. Therefore with the time out for nursing care, meals, visiting and so on, they get only about 15, 18 or perhaps 20 roentgens in a whole twenty-four hour period. If one were to give it intermittently with an x-ray tube one would deliver from 10 to 25 roentgens within a few minutes, which is considerably more of a shock to the organism, I believe. Total irradiation is a method which has come to stay in several fields of the radiosensitive diseases. In leukemia we have been more impressed with its results in chronic lymphogenous leukemia than in myelogenous leukemia. There are workers who maintain that with this method results can be obtained in the resistant case, the roentgen-fast case, of myelogenous leukemia; that is, the case with the big spleen that cannot be reduced any further with local irradiation. In these, total irradiation, they state, makes the spleen go down. I have never seen that happen, although I have no reason to doubt that it may take place in some cases. The result that impresses me is the effect on the blood count and not the effect on areas of lymphocytic or myelocytic infiltration. It has seemed to us that in lymphogenous leukemia we get results that are worth while, provided we do not carry the dose too far. I do not think we should exceed a total of 100 roentgens, which with the Heublein method would take about five or six days of treatment. We can discontinue whenever we see danger signals.

"GRANULOCYTOPENIA" VERSUS "AGRANULOCYTOSIS"

DR. FORKNER: I should like to say one more word in disagreement with Dr. Reznikoff about the use of the terms neutropenia or granulocytopenia, instead of agranulocytosis. Agranulocytosis is such an acute episode that I prefer the term acute agranulocytosis. It is not just neutropenia. There is a neutropenia in pernicious anemia, in Banti's syndrome, in malaria and in a great many other diseases, but I think agranulocytosis deserves a little more distinction than is suggested by the term neutropenia or granulocytopenia.

DR. REZNIKOFF: I am certainly in favor of distinguishing it, but we call it acute neutropenia. We put in the term "acute." The trouble in using agranulocytosis is that there are other cells that are granulocytes such as monocytes, and they are not always absent. But the distinctive feature of this acute condition is the fact that the principal cells which are depressed, and markedly depressed, usually below 10 per cent, are the neutrophils. I think it is also incorrect to use the term "angina."

DR. HARRY GOLD: I think the difference in terms used may have some bearing on the subject of therapy. Dr. Forkner said that about 70 per cent of patients with

acute agranulocytosis die, but it is my impression that in the group that would naturally fall under the designation granulocytopenia, the mortality is not nearly so high. Naturally it is the concept behind the names that matters. Most patients who have a low white blood cell count and a low neutrophil count and nothing else, I believe, recover. These could be considered cases of neutropenia or granulocytopenia. But Dr. Forkner has applied the term acute agranulocytosis to a condition which has a mortality of 70 per cent. Is there here only a difference in the severity of the disease or are some of the conditions included under the name neutropenia entirely different diseases bearing only superficial similarities to those included under the name acute agranulocytic angina? The reason I press the point is that the efficacy of a therapeutic agent can be evaluated only on the basis of the natural course of the disease or its mortality. The literature records several false steps in the attempts to treat so-called agranulocytosis. It is fairly easy to be misled in a disease which has a natural recovery rate of 70 per cent. The matter is otherwise in a disease with a natural mortality rate of 70 per cent. Which does this disease have?

DR. REZNIKOFF: The difference in the mortality figures for these conditions is due to the difference in the severity of the cases included in different groups that have been observed. Dr. Forkner and I refer to the same disease, although we prefer to apply different names to it.

DR. FORKNER: When I referred to the mortality of 70 per cent I had in mind not simple neutropenia but the more severe acute agranulocytosis.

DISCUSSION OF QUESTIONS

STUDENT: I should like to ask Dr. Forkner if platelets could not be used in leukemia as a possible diagnostic or prognostic index?

DR. FORKNER: Marked reduction or the absence of platelets in leukemia is on the whole a poor sign. One can expect less from therapeutic agents when the platelets are low in number. I think it is very important to consider them in treatment or in diagnosis, and no smear is adequately studied unless a statement is made about the platelets. Both in acute and in chronic uncomplicated lymphogenous leukemia there is a reduction in platelets. In myelogenous leukemia usually their number is normal or increased.

DR. MILHORAT: I gather that the basal metabolic rate is pretty important. What relation, if any, has the basal metabolic rate to the white count?

DR. FORKNER: Only in patients who have high white counts is there any relationship. A patient with leukopenia or with so-called subleukemic leukemia may have a very high basal metabolic rate. In that case there is no relation. But when a patient has a high white count the basal metabolism will vary more or less directly with the leukocyte count. A closer correlation is seen between the basal metabolic rate and the degree of immaturity of the cells.

DR. WALTER MODELL: Do you find arsenic of any value when the leukemic patient no longer responds to irradiation?

DR. FORKNER: Usually the patients who respond well to arsenic respond well to irradiation; those who take low doses of arsenic will take low doses of irradiation. Occasionally a patient will respond to arsenic

who will not respond to irradiation and vice versa, but that is not the rule. We have no indication of the mechanism by which arsenic is effective in leukemia. It is a good problem.

STUDENT: Is leukopenia a contraindication to the use of such substances as sulfanilamide, which are known at times to cause it?

DR. FORKNER: I do not think so, but you will find difference of opinion on that. If the leukopenia is due to sulfanilamide then put out the red flag, but if the leukopenia is due to the infection I do not think it is a contraindication to the use of sulfanilamide.

SUMMARY

DR. MILHORAT: Dr. Travell, will you add a few words in summary?

DR. TRAVELL: The conference today dealt with the therapy of two widely diverse groups of disorders of the white blood cells: those in which there is depression of the leukopoietic tissues on the one hand, and those in which there is excessive multiplication of the leukocytes, that is, the leukemias, on the other hand.

The terminology for the former group apparently needs some clarification, for the term agranulocytosis has been used to indicate an acute clinical syndrome which is usually fatal and also to apply to milder grades of granulocytopenia or neutropenia, from which the patient often recovers spontaneously. This uncertainty as to the expected mortality rate makes it difficult to evaluate the efficacy of the variety of therapeutic agents which have been used in the treatment of these conditions.

In agranulocytosis, granulocytopenia or neutropenia, the first aim of therapy is to remove the cause, and removal of the cause is usually all that is necessary to effect a cure. The etiologic factors include the use in hypersensitive individuals of certain drugs containing the benzene ring, such as aminopyrine, sulfanilamide, sulfapyridine and arsenicals, bacterial toxins, and x-rays and radium. In some instances the cause is obscure. The second aim of therapy is to stimulate the production and maturation of the granulocytes. For this purpose transfusions, liver extract and bone marrow stimulating agents, such as adenine sulfate and pentnucleotide, are of uncertain value. "Stimulating" doses of x-rays are of no value and may be dangerous.

The treatment of leukemia presents a different type of problem. It is generally believed that this is a neoplastic disease and, once initiated, removal of the cause would not in this case effect a cure. Although the patients with leukemia are rarely if ever cured, it is possible to relieve their symptoms. Remissions can be produced by suitable doses of x-rays or of arsenic or benzene. All of these measures tend to depress the bone marrow and thereby reduce the number of circulating white cells and the size of the tumor masses which are frequently the cause of symptoms. In the refractory stages of the disease a decrease in the number of white blood cells in the blood, however, is not always correlated with clinical improvement. It is possible that arsenic and irradiation may be combined with some advantage. Stress was laid on nonspecific measures which help to preserve the best possible state of well-being in the leukemic patient, such as the suitable restriction of activity, a high caloric diet, control of respiratory infections, attention to oral hygiene, and the avoidance of trauma because of the tendency to bleed. Probably the most important feature is the adaptation of therapy to the individual patient.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

CLARK HYDROTHERM NOT ACCEPTABLE

Manufacturer: Clark Electrical Equipment Company, Warren, Pa.

The Clark Hydrotherm, described in the advertising matter as a "humid air Fever Box," was not submitted to the Council for investigation; this report is based therefore on the advertising and promotional matter distributed by the firm.

A giant rubber hot water container, said to be 30 by 78 inches, called the Hydroelectric Mattress, appears to be the main feature of the device. As described in the advertising, "It is inflated with 10 gallons of water and air which is heated to any desired degree thermostatically. In the lower section of this mattress is a unique heating unit so designed as to operate as 'black heat' yet impart over the entire lower surface sufficient heat to raise the temperature of the water and air to any desired degree." It is claimed that "No other form of mattress construction offers the superb comfort which patients enjoy with our product. The patient floats upon this mattress as does a ship upon the sea."

This mattress is placed on a bed assembly. In the base of this assembly, a "unique vapor generator" is claimed to maintain a 75 per cent humidity in the cabinet. The enclosing cabinet or hood, on which are located various indicators and gages, is apparently used only when the temperature or fever is being induced. It is stated, "A very important feature is the fact that $\frac{1}{2}$ of the enclosing cabinet is mounted upon rollers so that it can be moved back over the foot end after the desired degree of fever is obtained. Fever can be maintained for any number of hours with cabinet moved back as the conduction of heat from the Hydroelectric Mattress is sufficient to hold the body temperature."

The advertising appears to be quite evenly proportioned between describing the mechanical virtues of the apparatus and its money-making possibilities. The physician is informed that "Producing results with fever will definitely expand your practice and income."

The following is quoted from promotional matter distributed by the firm:

"Here is a field, doctor, waiting—untouched—and the majority of these patients are prepared to pay well for definite results. You know that the average physician does not warm up to physical measures of heating—so-called machine medicine—yet FEVER is best developed by man-made methods and not with serums of foreign substances injected into the blood stream.

"With Government appropriation for a huge expansion of the Health program plus the present program to fight the spread of Venereal diseases—YOU have a virgin opportunity to step out front—become a leader in making FEVER available to those in your community who are waiting for some progressive doctor to install such a department.

"With the HYPOTHERM you can treat three to six patients per day—because you can develop a fever of 101 or 102 in less than 90 minutes—then after an hour's rest the patient can leave. These frequent passive treatments will be appreciated by hundreds who would rather come to YOUR OFFICE than go to a hospital—therefore Doctor—make room for this service; it will do more to PUT YOU OVER in your community than any investment you can make.

"Don't pass up this opportunity—don't say you haven't room—do as any businessman would do—MAKE ROOM for a profitable department—in a few years you'll be glad you did—people will be coming to you from far and near—we know they will be because we've sold our machines on the PAY OUT OF INCOME PLAN all during the depression and we know that doctors will pay us—when they are adding to their income—expanding their practice with our investment."

This promotion has the flavor of advertising copy used to distribute money-making amusement devices rather than professional equipment for a physician's office or a clinic. There

is even described a "meter-matic plan" whereby a certain number of coins are deposited in the apparatus each day until it is paid for.

The practice of fever therapy, in the opinion of the Council, should be limited to those who have been especially trained in this highly specialized field. Much instruction and practice in a fever clinic are required before such training is sufficient.

One piece of advertising, which appears to be a reprint, is titled "Pasturizing the Blood (Pyretotherapy with Conductive Heat)." On examination it is found that the author, said to be a well known physician, is not named, nor is the "leading medical journal" in which it is claimed that the article appeared.

The present Clark Hydrotherm, or Thermobath as it is sometimes called in the advertising, has superseded the more costly Clark Hyperpyrexator, according to the firm. Many unwarranted claims were made for the Clark Hyperpyrexator.

"Dr. Warren's Infra-Red Sitz Bath," marketed by Electrical Research Laboratories, was found not acceptable by the Council, as reported in THE JOURNAL, Sept. 14, 1935, page 881. According to correspondence and advertising, W. W. Clark is president of both the Electrical Research Laboratories and the Clark Electrical Equipment Company, and each is located in Warren, Pa. "Dr. Warren's Sitz Bath" consisted of a stool having a ringlike seat with a heating element in the base. It was claimed that this apparatus had many therapeutic benefits, and it was said to be a "Convenient and Effective Method of Rejuvenation," which would "Restore Physical Vigor." The device was advertised directly to the public.

The Council on Physical Therapy declared the Clark Hydrotherm not acceptable for inclusion in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

ANNUAL MEETING OF THE COUNCIL ON PHARMACY AND CHEMISTRY

The Council on Pharmacy and Chemistry of the American Medical Association held its thirty-fifth annual meeting at the Association headquarters March 8-9, 1940. Those in attendance were Drs. David Barr, J. Howard Brown, S. W. Clausen, H. N. Cole, C. W. Edmunds, Morris Fishbein, E. M. K. Geiling, Paul Nicholas Leech, Perrin H. Long, G. W. McCoy, Stuart Mudd, E. M. Nelson, W. W. Palmer and Elmer L. Sevringhaus. In addition, the following members of the Council on Foods attended the meeting: Dr. George R. Cowgill, Dr. Arild E. Hansen (proxy for Dr. Irvine McQuarrie), Mr. Culver S. Ladd, Dr. James S. McLester, Dr. Tom D. Spies, Dr. Russell M. Wilder and Dr. Franklin C. Bing. Dr. Torald Sollmann was reelected chairman of the Council and Dr. W. W. Palmer was reelected vice chairman.

Among the many items discussed, the following may be of interest both to physicians and to manufacturers:

Use of Term "Digitalis Unit."—The Council voted that a special committee be appointed to consider in extenso the digitalis unit and report back to the Council. In the discussion it was emphasized that digitalis, or anything that purports to be digitalis, is an official drug and, by that token, it must be standardized according to the methods laid down by the U. S. Pharmacopeia. If there is a demand for another standard, that standard may appear on the label in addition to the U. S. P. standard, provided the labeling of the second standard is not misleading. It was also emphasized that representations may be made to the U. S. Pharmacopeial Revision Committee for reconsidering the standards of digitalis preparations if that is necessary.

Councils' Committee on Contraceptives.—The Councils' Committee on Contraceptives made a progress report concerning certain articles that have been authorized for publication. The

Council voted that certain recommendations of the Committee be adopted by the Council on Pharmacy and Chemistry and referred to the Board of Trustees for action.

Change of Name "Thiamin Chloride."—The Council voted to adopt the pharmacopeial term "thiamine hydrochloride" to replace the term suggested by the discoverer, i. e. "thiamin chloride." The manufacturers of accepted preparations, however, will be given a suitable period of time in which to use up the old labels bearing the name "thiamin chloride."

Proposed Articles on Glandular Therapy and Physiology.—The Council received a report from the committee in charge of the proposed new series of articles and authorized the Secretary's office to approach certain persons with the request that they contribute to this series.

Present Status of Pneumonia Therapy.—It was pointed out that the difficult question at the present time in determining the preferred treatment of pneumonia is whether or not the best plan is to use sulfapyridine alone, serum alone, or serum and sulfapyridine. It was the general consensus that there is not sufficient information yet available to determine the value of combined serum and sulfapyridine compared with adequate serum therapy alone or with adequate sulfapyridine therapy alone. Furthermore, there enters into the equation the relative cheapness of sulfapyridine therapy in comparison with serum therapy. It was the general consensus of the Council members that the practice of typing should be continued for information, both in relation to treatment and for statistical purposes. In early cases of pneumonia and when typing has been employed it is probably best to give a specific antipneumococcic serum, at the same time (followed by the specific carbohydrate test to determine if the serum is present in sufficient amounts), this to be followed by the use of sulfapyridine, with the caution not to stop the administration of sulfapyridine too soon in order to avoid late complications. This statement, however, is to be looked on simply as a tentative statement based on the present evidence. As further data become available the Council will be in a position to make more positive statements.

The Council also voted to accept type III rabbit antipneumococcic serum for a period of one year only, and authorized publication of a report to the effect that the higher types of rabbit antisera are under consideration. Furthermore, the Council will consider with the view to acceptance the carbohydrate material for skin testing and treatment in conjunction with antipneumococcic serums (Francis test).

Solution of Zinc Insulin Crystals.—The Council concluded that a statement should be prepared announcing recognition of solution of zinc insulin crystals for inclusion in New and Nonofficial Remedies.

Antiseptics, Bacteriostatic Agents, Preservatives and Disinfectants.—The Council again considered the problems relating to these preparations and the misunderstandings which arise concerning these terms. At the same time it again discussed the inadequacy of the phenol coefficient test for the evaluation of antiseptics and disinfectants. The referee was authorized to formulate a report for the consideration of the Council and, if possible, to consult with the federal authorities concerned with these questions.

Catgut Suture Investigation.—A progress report was made concerning the further investigation of catgut sutures. It is anticipated, however, that another year of investigation will be required before the Council may be in a position to publish the results of the work which is being undertaken under its auspices.

Advertising Brochures.—The Council discussed the question of the increasing number of large size brochures dealing with proprietary drugs. In this form of advertising the commercial houses take on themselves the task of educating the physician in the fields to which their products pertain. For instance, a recent brochure contained no less than sixty drawings of surgical procedures; others attempt to cover in elaborate detail such fields as those of endocrine or vitamin therapy. (The writers of these enlarged pamphlets discuss as many usages as possible for the product which they are promoting.) Some

members of the Council felt that this type of advertising material is not to be commended and that pharmaceutical houses should confine their advertising material to less lengthy descriptions of the product and the technic used. On the other hand, it was pointed out that in some restricted fields textbooks on therapeutic problems are not sufficiently up to date and that in such instances these brochures may fill a need. It was voted that a special committee be appointed to inquire into the matter of advertising brochures and report to the Council, especially in regard to the abuses.

Pharmacopeial Convention.—The Council members discussed the forthcoming pharmacopeial convention with a view to enlisting the aid of the medical interests to attend the convention in order that good progress might be made in the final elaboration of the next pharmacopeia.

Rearrangement of Articles on Serums and Vaccines.—The Council members voted to revise and rearrange the New and Nonofficial Remedies chapter on serums and vaccines.

So-Called Lipoid Pneumonia.—The Council authorized a review to be made of the lipoid pneumonia problem, on the basis of which the Council might again consider what action to take in the case of nasal sprays in which liquid petrolatum is the vehicle.

Therapeutic Research.—The Council voted that the Committee on Therapeutic Research be thanked for its painstaking effort and for the active productivity of the work which it fosters. The report of the committee appears in the annual Reports of Officers, THE JOURNAL, May 11, 1940, p. 1918.

Permissible Claims for Vitamins.—The Council considered the "Status of Permissible Claims for Vitamins" as given in New and Nonofficial Remedies. It was the opinion of the Council that with a few exceptions these claims as they stood were applicable today. The Council ordered, however, that revisions be made in the permissible claims for riboflavin, nicotinic acid and pyridoxine (vitamin B₆), and that after the referees for these preparations have sent in their proposed alterations these be passed on by the Cooperative Committee on Vitamins with the view of later publishing a revised edition of the pamphlet entitled "The Status of Certain Questions Concerning Vitamins," and concordant revision of the statements in New and Nonofficial Remedies.

Nomenclature of Vitamins.—The Council voted to accept the terms "pyridoxine" and "pyridoxine hydrochloride" for the substances known as vitamin B₆ and vitamin B₆ hydrochloride, provided the nomenclature met with the approval of the American Society of Biological Chemists and the American Institute of Nutrition. The meetings of these organizations were to follow that of the Council (an official announcement of the Council on these names was published in THE JOURNAL, June 15, 1940, p. 2387).

The Council also discussed the term "halibut liver oil with viosterol" for a product containing halibut liver oil with viosterol and other fish liver oils. Such preparations have generally been diluted with cod and other fish liver oils to adjust the vitamin A content. The addition of such oils to a product sold under the labeled name "halibut liver oil with viosterol" will make the product subject to action under the misbranding provisions of the Federal Food, Drugs and Cosmetic Act even though the presence of the added ingredients is declared elsewhere on the label. The present definition for halibut liver oil with viosterol, as given in New and Nonofficial Remedies, is as follows:

Halibut liver oil to which has been added sufficient viosterol (irradiated ergosterol) to assure a potency of not less than 10,000 vitamin D units (U. S. P.) per gram; the halibut liver oil used is adjusted (when necessary) to have a vitamin A potency of not less than 44,800 units (U. S. P.) of vitamin A per gram by the addition of fish liver oils from one or more of the species *Gadus morhua*, *Ophiodon elongatus* and *Anoplopoma fimbria*.

The Council voted that this be changed and that the definition of the future editions of the New and Nonofficial Remedies be:

Halibut liver oil-N. N. R. to which has been added sufficient viosterol (activated ergosterol) to assure a potency of not less than 10,000 U. S. P. units of vitamin D per gram.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JULY 13, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

CHEMICAL CHANGES IN THE BLOOD

The value of an understanding of the chemical changes that take place in the blood in disease has long been recognized. The data obtained as a result of biochemical analysis serve to supplement the information which the clinician may obtain in other ways. At present means exist for determining more completely than ever before changes in the blood that are encountered in disease. Ample application in the various branches of medicine is found, moreover, for all the knowledge obtainable concerning deviations from the normal in protein, carbohydrate, fat or inorganic metabolism as well as for aberrations of endocrine, renal or hepatic function. The literature dealing with clinical biochemistry is extremely voluminous; reports which discuss and correlate the results of investigative activity in this field are therefore welcome. In a recent review of this type, Myers and Muntwyler¹ draw attention to devel-

opments of the past few years with regard to chemical changes in the blood and to the clinical significance of these changes.

The clinical significance of wide excursions from the normal of the sugar content of blood is evident, yet many of the methods used to determine this constituent are rather nonspecific. Even the values obtained with the aid of the widely used Folin-Wu method are actually much higher than the values for the true sugar content of blood. With the help of methods now available, the true sugar content can be accurately determined. In estimations giving normal or elevated values, however, it is considered by many to be unnecessary to employ methods yielding the true blood sugar values, and procedures such as that of Folin and Wu are still commonly employed. In the latter case, of course, the limitations of the method are properly considered in the interpretation of the analytic results. However, when hypoglycemic blood is examined for sugar it is important to know its true carbohydrate content, because in this case the error occasioned by the presence of non-sugar reducing materials in blood is relatively great.

Variations which occur in the lipid content of blood in normal pregnancy, diabetes, certain renal conditions and pernicious anemia are comparatively well known and appreciated. In recent years the value of plasma cholesterol estimations in thyroid disease has been investigated² and the usefulness of plasma cholesterol and cholesterol ester determinations in liver disease has been emphasized.³ The association of hypercholesterolemia and hyperbilirubinemia in obstructive jaundice has likewise received attention.⁴ The serum pigments themselves have been of interest for many years and both the icterus index and the van den Bergh reaction have found extensive clinical use. The possible influence of carotenemia on the icterus index has merited notice, and some time ago Nation and Myers⁵ came to the conclusion that only in cases of marked carotenemia, such as might be encountered in some diabetic patients, is the validity of the icterus index affected. Carotenemia observed in patients with diabetes mellitus may be due to the inability of the organism to convert carotene to vitamin A.⁶

With regard to the proteins in blood, it is interesting to note that the gasometric method of Van Slyke for the determination of the oxygen capacity, and hence the hemoglobin content, of blood has proved extremely useful. The simplicity of the method has also made it admirably suited to checking standards used in the determination of hemoglobin by colorimetric methods.

2. Hursthal, L. M.: Blood Cholesterol in Thyroid Disease: Analysis of Findings in Toxic and Nontoxic Goiter Before Treatment, *Arch. Int. Med.* 54: 22 (Jan.) 1933.

3. Epstein, E. Z.: Cholesterol Partition of Blood Plasma in Parenchymatous Diseases of Liver, *Arch. Int. Med.* 47: 82 (Jan.) 1931; Cholesterol of Blood Plasma in Hepatic and Biliary Disease, *ibid.* 50: 203 (Aug.) 1932.

4. Epstein, E. Z., and Greenspan, E. B.: Clinical Significance of Cholesterol Partition of Blood Plasma in Hepatic and in Biliary Disease, *Arch. Int. Med.* 58: 860 (Nov.) 1936.

5. Nation, E. F., and Myers, V. C.: Carotenemia: Its Influence on Validity of Icteric Index, *Proc. Soc. Exper. Biol. & Med.* 31: 117 (Feb.) 1934.

6. Hazer, J. G., and Curtis, A. C.: Vitamin A Deficiency in Diabetes Mellitus, *Arch. Int. Med.* 65: 90 (Jan.) 1940.

1. Myers, V. C., and Muntwyler, E.: Chemical Changes in Blood and Their Clinical Significance, *Physiol. Rev.* 20: 1 (Jan.) 1940.

and directly or indirectly the gasometric procedure has facilitated the accumulation in all parts of the world of a vast amount of accurate information on the hemoglobin concentration of human blood. The value of estimations of serum proteins in the various forms of renal disease is generally recognized, and of late considerable attention has been paid to serum colloid osmotic pressure. Concerning the nonprotein nitrogen constituents of blood, Myers and Muntwyler indicate that nonprotein and urea nitrogen are probably still regarded as furnishing more information of diagnostic or prognostic import as far as the kidneys are concerned than any other single determination, although elevated values may sometimes be attributed to other causes. Regarding renal function tests a comparison of the blood urea clearance test with the blood urea and blood creatinine content alone, as well as with the phenolsulfonphthalein test, shows that the blood urea clearance usually falls below 50 per cent of its normal value before any of the other three values shows any abnormality.⁷ The employment of the blood urea clearance test as a reference test in studies of renal function seems to be amply justified. The uric acid content of blood continues to receive attention, particularly in connection with gout, and the possible clinical importance of guanidine in the blood has attracted renewed interest with the development of an improved method for its determination. High values for guanidine in blood have been reported among other conditions in severe toxemias of pregnancy, in cases of epilepsy and in some cases of liver disease.

In addition to a consideration of the organic constituents of blood, the various inorganic materials have been increasingly studied in health and disease. Changes in the blood with regard to its content of sodium, potassium, magnesium and calcium among the cations and of bicarbonate, chloride and phosphate among the anions, in particular, are encountered in numerous clinical conditions. Even enzyme determinations are found to be clinically significant. Thus, estimations of plasma phosphatase activity are of especial value in the detection of latent or active rickets.

Each patient presents a problem which cannot be appreciated solely on the basis of dissociated laboratory studies.⁸ Moreover, if any value is to be attached by the clinician to information obtained by the chemical analysis of blood it is imperative that he be fully aware not only of the significance which the results might have but also of the limitations of the methods used to supply the information. However, when properly interpreted a knowledge of chemical changes in the blood as revealed by analytic methods is of much clinical value. With the advent of a fuller understanding of the changes that occur in the blood in disease, the position of the laboratory as a helpmeet in medicine may be even more prominent than it is now.

7. Van Slyke, D. D., and others: Studies of Urea Excretion: Comparison of Blood Urea Clearance with Certain Other Measures of Renal Function, *J. Clin. Investigation* 5: 357 (April) 1930.

8. Cantarow, Abraham, and Trumper, Max: *Clinical Biochemistry*, ed. 2, Philadelphia, W. B. Saunders Company, 1939.

POSTGRADUATE TRAINING IN CRIMINAL PSYCHIATRY

A Pennsylvania fellowship plan for intramural training in penal psychiatry has been formulated,¹ pursuant to recommendations of the Medical Society of the State of Pennsylvania,² by a joint medicolegal committee of the Philadelphia County Medical Society and the Philadelphia Bar Association. The plan has already been endorsed by the Philadelphia Psychiatric Society, the Pennsylvania Psychiatric Society, the College of Physicians of Philadelphia and the board of directors of the Philadelphia County Medical Society.

The joint medicolegal committee recognizes the need for education of the criminologist as well as rehabilitative education of the criminal offender. By its plan it hopes to provide an educational institution for the training of personnel and the development of quality research in the field of penal psychiatry and thus render more probable of success any scientific remedies which the state legislature may or has set up for various aspects of crime. The committee believes that its plan satisfies the essentials for training qualified persons in criminal psychiatry since it contemplates (1) the creation of fellowships in penal psychiatry, (2) the use of penal and correctional institutions as clinical laboratories and (3) the identification of the fellowships with some institution of learning.

The Pennsylvania plan is to be administered by a committee representing three departments of the University of Pennsylvania—the Department of Psychiatry, the Graduate School and the Law School—and the Eastern State Penitentiary. The fellowships are for a term of two calendar years and carry stipends of \$2,600 the first year and \$3,000 the second year, with additional allowances for clerical services. To qualify for such a fellowship a candidate must (1) be a male not over 35 years of age, (2) be a graduate from an accredited medical school, (3) have served an accredited internship, (4) possess a sound psychiatric background consisting of at least two years of acceptable previous psychiatric training and (5) possess acceptable character endorsements. The tentative curriculum prescribed for a fellow consists of study in the law, medical and graduate schools of the University of Pennsylvania, experience and observation at the Eastern State Penitentiary and in the courts, and participation in intramural clinical psychiatric problems related to classification, discipline, rehabilitative treatment and parole of criminals.

The committee is confident that its plan will not only accomplish its primary purpose of training competent personnel in criminal psychiatry but also improve the

1. Report on the Pennsylvania Plan (Intramural Training in Penal Psychiatry), Joint Medico-Legal Committee of the Philadelphia County Medical Society and the Philadelphia Bar Association, March 1940.

2. Minutes and Proceedings of the Eighty-Ninth Annual Session of the Medical Society of the State of Pennsylvania, Pittsburgh, Oct. 2-5, 1939, approving the Report of the Committee on Psychiatric Services to the Criminal Courts, *Pennsylvania M. J.* 42: 293 (Dec.) 1939.

general status of psychiatric expert testimony and bring closer together the legal and medical professions, the University of Pennsylvania and state penal institutions to the end that all four may more effectively serve the needs of the community. The committee is to be commended for its timely efforts in blazing this much needed trail in the field of penal psychiatry.

Current Comment

EXPERIMENTS IN CANCER REPORTING

More than 12,000 cases of cancer have been reported since January to the Division of Cancer Control of the New York State Department of Health, according to a press release¹ dated May 27. This has come about through "prompt and adequate response of the medical profession in upstate New York in reporting cancer under the new cancer reporting law." Health department officials regard this as the first successful venture of its kind anywhere in the country and probably in the world. The reports are made by physicians, hospitals and laboratories and are of increasing scientific value because in more than 70 per cent of cases they are accompanied by data from the pathologic laboratory regarding the microscopic character of the tumor. These cancer reports are being handled "with the greatest possible care with respect to their confidential nature and they will be used for scientific analysis only." Unexpectedly, benign tumors and other benign conditions are being reported to the extent of more than a thousand cases a month; these reports may be of use in establishing statistical information as to how frequently a malignant condition may supervene in apparently benign growths. The practical working of a law requiring reports of a noncommunicable disease for statistical, educational and control purposes will be watched with interest by physicians everywhere. Already it is stated that the number of cases reported "compares favorably with results obtained in the past by expensive special surveys carried out to gather similar data."

HONORING DR. S. BURT WOLBACH

The current July issue of the *Archives of Pathology* is dedicated by his present and former pupils and associates to Dr. S. Burt Wolbach, of Harvard Medical School, where for thirty years he has served, in a distinguished manner, first as assistant professor and later as associate professor of bacteriology, then as associate professor of pathology and bacteriology, and since 1922 as Shattuck professor of pathology. In this large issue of the *Archives* are numerous scientific papers which indicate the broad field of study in which Professor Wolbach's students and associates have engaged and the far-reaching effect of his stimulating leadership in this field. Although for twenty years he has been pathologist to the Peter Bent Brigham Hospital and for a longer period

to the Boston Children's Hospital, and to other hospitals, he also has vigorously carried on with his associates numerous researches, some of which disclose previously unappreciated opportunities for cooperation with workers in other fields. Especially notable are his researches on typhus, Rocky Mountain spotted fever, and the vitamins. Most interesting is the sketch of Dr. Wolbach's career, written by Prof. Walter B. Cannon as an introduction to this special issue. Dr. Wolbach, now 60 years of age, was born at Grand Island, Neb., where his early years were spent on the range in association with alert and hardy men whose enterprise helped to build Western civilization. Horseback riding today remains one of his chief recreations. To see Burt Wolbach and his favorite horse, Professor Cannon says, is a beautiful revelation of both human and equine nature. A morning ride, rain or shine, still keeps him physically fit for the strenuous work of the day—teaching, attending routine duties in school and hospitals, eagerly engaged in various research, and fulfilling his deep sense of obligation by guiding his disciples along old paths and toward fresh ventures in pathology. Wherever he has labored in hospitals and laboratories—in Boston, in Albany and in Montreal—his kindness and helpfulness have made for him devoted friends.

PULMONARY TUBERCULOSIS AFTER HEALED PRIMARY COMPLEX

A recent report by Fellows,¹ based on serial chest roentgenograms of 3,179 office employees from 1926 to 1938, introduces interesting evidence regarding the pathogenesis of tuberculosis. Fellows divided the group into those whose x-ray examinations showed (1) an average healthy or normal chest, (2) an apparently healed primary complex, and (3) a lesion requiring further study. In calculating the comparative incidence of the development of tuberculosis in the first two groups, the number of years of life under observation at each year of age was tallied by sex and note was made of the age at which tuberculosis was first detected. There were 2,536 persons in the average healthy or normal chest group and 449 in the healed primary complex group. Fifty in the first group acquired tuberculosis subsequent to this first roentgenogram; seven in the second group, whose first roentgenogram showed healed primary complex, also acquired tuberculosis. Thus it appeared that there was no greater tendency toward tuberculosis in those with healed primary complex than in those with chests roentgenographically normal. Moreover, it was clearly apparent from the entire study that apparently healthy working adolescents and adults frequently have conditions and diseases in the lungs which are unrecognized by the usual clinical examination and that an examination of the lungs cannot be considered complete without a fluoroscopic or roentgenographic examination. The latter conclusions have now been so thoroughly substantiated in numerous studies that they can be considered, for practical purposes, as clinically proved.

1. New York State Dept. of Health, Albany, N. Y., News Service, May 27, 1940, Edward S. Godfrey Jr., M.D., commissioner.

1. Fellows, H. H.: *J. Indust. Hyg. & Toxicol.* 22:157 (May) 1949.

MEDICAL PREPAREDNESS

In this section of *The Journal* each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

QUESTIONNAIRE FOR MEDICAL ENROLMENT

On this page appears a facsimile, greatly condensed, of a questionnaire which is now being sent to every licensed physician in the United States and in all its territories. This questionnaire is being sent at the request of the Surgeon Generals of the United States Army, Navy and Public Health Service as part of the plan for preparedness of the medical profession to enable our country to meet any emergency which may arise. The questionnaire was developed with the advice and assistance of the members of the Committee on Medical Preparedness and of the Surgeon Generals. Just as soon as these questionnaires are received in the headquarters office of the American Medical Association the information supplied will be transferred to cards in a punch card system, so that it will be possible by the use of the usual machines to make a selection of physicians capable of serving in various military, naval, industrial or civil capacities.

The physician who receives this questionnaire should take the necessary time and give the necessary thought to supplying a complete and absolutely correct reply. It is the desire of the authorities, should an emergency arise, to place every individual capable of rendering aid in the position in which he can be of the utmost service, and also naturally where his training and his experience most definitely qualify him. It will be observed that opportunity is offered to state appointments in hospitals, together with the nature of the appointment, membership in special medical organizations, together with the nature of such membership, and whether or not the physician possesses the certificate of one of the examining boards in the medical specialties. There is also opportunity to provide complete information concerning the civil status of the physician concerned, whether or not he practices alone or in association with other physicians, whether

or not he is married and has children, and whether or not he has any physical incapacity which might prevent him from doing certain types of service.

It is hoped that every physician will cooperate with the Committee on Medical Preparedness and with the United States government by filling out this blank and returning it at the earliest possible moment. Obviously, as physicians are needed, an attempt will be made to supply them through this mechanism. If conscription should become necessary, every effort will no doubt be made to assign physicians to work for which they are especially suited. Those who have failed to cooperate will naturally take the chance of being assigned to any kind of service which may offer, and perhaps with far less possibility of rendering the quality of aid they are capable of rendering. When Canadian physicians were requested to provide similar information more than 90 per cent volunteered to serve in any capacity to which they should be assigned. Our medical profession has always enrolled itself among the leaders in patriotism and love of our country.

Cooperation and preparedness at this time constitute the duty of every American citizen who enjoys his citizenship and wishes to preserve the American democracy.

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ORGANIZATION SECTION

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 5874 has been reported to the House, proposing to include the name of Gustaf E. Lambert among those honored by an act recognizing the high public service rendered by Major Walter Reed and those associated with him in the discovery of the cause and means of transmission of yellow fever. The Senate rejected a proposed amendment to the Revenue Act of 1940 which would have exempted from the increased tax on distilled spirits all alcohol used exclusively for manufacturing drugs. Senator McKellar, Tennessee, in submitting this amendment stated that one of the principal ingredients in all "patent medicines" is alcohol and that "'patent medicines' are the poor man's doctor."

Bills Introduced.—S. 4179, introduced by Senator Walsh, Massachusetts, provides for the establishment of a National Physical Fitness Institute in the Federal Security Agency. The institute will be authorized, if the bill is enacted, to (1) select, prepare and conduct research with respect to tests and testing instruments for the purpose of testing physical fitness; (2) select, prepare and conduct research with respect to follow-up procedures, forms of reports, and methods of cooperating with agencies engaged in medical and health work, for the purpose of conserving and increasing the physical fitness of the American people; (3) conduct research for the purpose of determining

the most efficient and practical methods of conserving and increasing physical fitness; (4) train specialists in the work of conserving and increasing physical fitness; (5) prepare reports and bulletins with respect to the conservation and increase of physical fitness for use by organizations and the general public; (6) on request, investigate the needs of organizations and industries for and, to the extent possible with its personnel, cooperate with such organizations and industries in providing physical fitness services for their members and employees, and (7) cooperate with departments and other agencies of the government in programs designed to conserve and increase the physical fitness of their officers and employees. H. R. 9951, introduced by Representative Edelstein, New York, proposes to provide workmen's compensation for employees of carriers engaged in interstate transportation by motor vehicles. The duty is to be devolved on the employer to furnish such medical, surgical and other attendance or treatment, nurse and hospital service, medicine, crutches and apparatus for such period as the nature of the injury of the employee or the process of recovery may require. All fees and other charges for such treatment or service will be limited to such charges as prevail in the same community for similar treatment of injured persons of like standard of living and will be subject to regulation by the deputy commissioner of the United States Employees' Compensation Commission having jurisdiction in respect of an injury.

OFFICIAL NOTES

ABSTRACT OF MINUTES OF MEETINGS OF BOARD OF TRUSTEES HELD IN NEW YORK CITY, JUNE 9-13, 1940

A full day meeting of the Board was held on Sunday, June 9, and meetings of shorter duration were held each day from Monday to Thursday inclusive of the week of the annual session. Some of the deliberations of the Board are reflected in the following actions. Other matters too numerous to mention were discussed.

NATIONAL PREPAREDNESS

A special committee appointed for the purpose brought in a resolution suggesting the creation of a Committee on National Preparedness, whose duty it would be to establish and maintain contact and suitable relationship with all governmental agencies concerned with the prevention of disease and the care of the sick, in both civil and military aspects, so as to make available at the earliest possible moment every facility that the American Medical Association can offer for the health and safety of the American people and for the maintenance of American democracy.

The Board approved the necessary expenditure for the compilation of information relative to the physicians of the country which can be made available to the government.

INDICTMENT OF ASSOCIATION

Dr. Olin West, Secretary and General Manager of the American Medical Association, was authorized to appear before the United States District Court for the District of Columbia on Friday, June 14, to enter a plea of not guilty for the Association in the case of the United States vs. the Medical Society of the District of Columbia, Harris County Medical Society, certain members of the Medical Society of the District of Columbia and certain members of the administrative personnel of the American Medical Association. Dr. Fishbein was authorized to enter the plea of not guilty in the event that Dr. West could not do so.

CHANGE IN NAME AND POLICIES OF COUNCIL ON FOODS

The Board approved the change in name of the Council on Foods to Council on Foods and Nutrition and a change in its policies so as to concentrate its efforts on the important function of expressing authoritative group opinion on foods and the nutritional claims made for them, and to avoid effort that would duplicate the activities of the Federal Food, Drug and Cosmetic Administration.

REPRESENTATIVES OF ASSOCIATION TO OTHER ORGANIZATIONS

Dr. Fishbein was appointed a member of the Committee on Education and the Committee on Publications of the National Foundation for Infantile Paralysis.

Dr. W. W. Bauer was authorized to continue to serve for another two years as a member of the General Advisory Committee on Maternal and Child Welfare Services to assist in the development of sound working relationships between the federal government and the states in the extension and improvement of health and welfare services for the mothers and children of the United States.

Mr. Howard A. Carter, Secretary of the Council on Physical Therapy of the American Medical Association, was appointed as alternate representative of the American Medical Association on the Committee on Acoustical Measurements and Terminology of the American Standards Association. Dr. Austin A. Hayden is the representative of the American Medical Association on that committee.

Dr. George M. Lyon, of Huntington, W. Va., was appointed to succeed Dr. Edward Jackson on the Joint Committee on Health Problems in Education of the American Medical Association and the National Education Association.

Dr. W. W. Bauer was appointed to serve as a member of the Year Book on Health Education for the American Association of School Administrators.

STANDARD CLASSIFIED NOMENCLATURE OF DISEASE

The following physicians were appointed to constitute the Editorial Advisory Board of the Standard Classified Nomenclature of Disease: Drs. George Baehr, Dana W. Atchley, Neil A. Dayton, Bowman C. Crowell, Christopher G. Parnall, Halbert S. Dunn and James R. Miller, with Dr. E. P. Jordan as Chief Editor.

ABSTRACT JOURNAL COVERING CLINICAL MEDICINE AND SURGERY

Further consideration of the publication of an abstract journal of clinical medicine and surgery by the Association was postponed for the reason that the publication of some foreign periodicals seems to have been suspended on account of the disturbing conditions abroad and that others are not being received at regular intervals.

RED CROSS SOCIETIES TO REPRODUCE ARTICLES FROM HYGEIA

Permission was granted to the League of Red Cross Societies, Geneva, Switzerland, to reproduce or summarize in their Red Cross magazines articles appearing in *HYGEIA*.

OFFICERS OF BOARD OF TRUSTEES FOR ENSUING YEAR

The following officers and committees were elected for the ensuing year: Chairman, Dr. Arthur W. Booth; Secretary, Dr. Austin A. Hayden; Executive and Finance Committee: Drs. Bloss, Sensenich and Hayden; Committee on Scientific Exhibits: Drs. Cullen, Henderson and Lee.

RESOLUTION IN HONOR OF DR. CHARLES B. WRIGHT

A resolution on the death of Dr. Charles B. Wright, who had been a member of the Board for seven years and who had served as Chairman of the Executive Committee for three years, was adopted for presentation to the House of Delegates.

WOMAN'S AUXILIARY

Arkansas

Dr. T. P. Foltz spoke on "Should Medicine Be Socialized on a National Scale?" at a joint meeting of the auxiliary to the Sebastian County Medical Society and the Parent-Teacher Association in Fort Smith, March 7.

At an open meeting arranged by the auxiliary to the Pulaski County Medical Society at the University of Arkansas School of Medicine, Little Rock, February 21, Dr. A. S. Buchanan, president of the Arkansas Medical Society, spoke on socialized medicine and Mrs. C. E. Kitchens, president of the auxiliary, spoke on the life of Jane Todd Crawford.

California

One hundred and seventy-nine members and guests attended the regular meeting of the auxiliary to the Los Angeles County Medical Association in Long Beach, February 27. Capt. Joel T. Boone, U. S. Navy, was the speaker.

Mr. F. J. O'Ferrall, Chief Inspector of the State Division of Narcotic Enforcement, addressed the auxiliary to the Fresno County Medical Society, February 6.

At a meeting of the auxiliary to the Marin County Medical Society held in Fairfax, February 22, Mr. Robin Lampson summarized his book, "Death Loses a Pair of Wings," a story of the life of Dr. William C. Gorgas.

Mrs. Julian Jacobson reviewed "Life and Death: The Autobiography of a Surgeon," by Andrea Majocchi, at a meeting of the auxiliary to the Santa Cruz County Medical Society, February 26.

District of Columbia

The auxiliary to the Medical Society of the District of Columbia held its annual reception in Washington, January 23, under the presidency of Mrs. Robert M. Bolton. Mrs. V. E. Holcombe, president-elect of the auxiliary to the American Medical Association, was guest of honor.

The auxiliary has helped the Red Cross by copying braille manuscripts and by making surgical dressings for patients. It has raised money for the Orthopedic Clinic of the Children's Hospital and for the "Incubator Fund," the purpose of which is to place incubators in all the hospitals in the District of Columbia. The auxiliary has contributed clothing and household goods to the Self-Help Exchange, toys and gifts to children at the Heart Clinic and a radio to the Children's Hospital.

Illinois

At the March meeting of the auxiliary to the Chicago Medical Society Mrs. Jesse R. Gerstley talked on "Recent Escape Literature." At a meeting of the auxiliary, April 3, Dr. Rollo K. Packard spoke on "Hospital Facilities and Needs in the United States." Special guests were Mrs. Rollo K. Packard, president, auxiliary to the American Medical Association, Mrs. Eben J. Carey, chairman, *Hygeia* committee, auxiliary to the American Medical Association, and Mrs. Oscar W. Friske, past president, auxiliary to the State Medical Society of Wisconsin. At a meeting of the North Shore Branch of the auxiliary to

the Chicago Medical Society on April 1 Dr. C. J. Barborka was speaker.—Mrs. Olive Bruner, principal of the Spalding School for Crippled Children, spoke on the subject "The Crippled Child in School" at the March meeting of the auxiliary to the Irving Park Branch of the Chicago Medical Society.—Mrs. Bernice Vandervries, representative, Sixth Congressional District of Illinois, discussed the duties of a representative and the importance of voting at the March meeting of the auxiliary to the Aux Plaines Branch of the Chicago Medical Society.

Mrs. Charles C. Winning, president, auxiliary to the Illinois State Medical Society, discussed the aims of the auxiliary at the charter meeting of the auxiliary to the Peoria County Medical Society, March 5. Fifty-seven women signed the charter of the newly formed auxiliary. At the following meeting, April 2, members discussed the Wagner Health Bill.

Dr. Elizabeth Ball, Department of Public Health, State of Illinois, discussed "Health, Weight and Diet" at a public relations meeting of the auxiliary to the Knox County Medical Society in Galesburg, March 22.

The county health program was discussed at a meeting of the auxiliary to the Adams County Medical Society in Quincy, March 11. Dr. James H. Hutton, president of the Illinois State Medical Society, spoke on "Some Important Facts All Auxiliary Members Must Know" at a meeting of the auxiliary in Quincy, April 8.

Indiana

Thomas A. Hendricks, executive secretary, Indiana State Medical Association, spoke on socialized medicine before the auxiliary to the Tippecanoe County Medical Society, Lafayette, March 12.

Kansas

The auxiliary to the Labette County Medical Society met in Parsons, January 24. A paper on the life of Florence Nightingale was read by one of the members.

The auxiliary to the Wyandotte County Medical Society met in Kansas City, January 12. Miss Viola Garret gave an account of her vacation trip through the Scandinavian countries.

Oklahoma

The auxiliary to the Le Flore County Medical Society sponsored programs on socialized medicine for the Parent-Teacher Association with addresses by Dr. Rush Wright and Mrs. Loton Shippey, president of the auxiliary, in Poteau recently. In February, the auxiliary and the Federation of Women's Clubs held a joint meeting for the public on cancer control in Poteau, at which time Dr. J. S. Binkley, of New York, was the speaker.

The auxiliary to the Tulsa County Medical Society placed *Hygeia* in all the public schools of Tulsa County. The auxiliary purchased a new short wave diathermy apparatus for the Tulsa County Medical Clinic recently and has made and distributed a large number of garments for infants.

The auxiliary to the Pottawatomie County Medical Society placed copies of *Hygeia* in all rural communities adjacent to Shawnee.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

State Medical Election.—Dr. Samuel A. Gordon, Marion, was elected president of the Medical Association of the State of Alabama at its recent annual meeting. Drs. Merle E. Smith, Parrish, and Douglas L. Cannon, Montgomery, were reelected vice president and secretary-treasurer, respectively. Mobile was selected for the next annual session, April 15-17, 1941.

CALIFORNIA

Restriction of Sale of "Sleeping Potions."—To reduce the death toll from drugs heretofore purchased without restrictions, the state board of pharmacy adopted a resolution prohibiting the sale of dangerous sleeping potions, according to the *Los Angeles Times*. Since January 1 there have been twenty-three deaths in Los Angeles and vicinity and seven in the San Francisco area, either through suicide or accident, as a result of promiscuous purchase of deadly drugs, it was stated. The state department of public health took similar action, May 25, its resolution naming as dangerously poisonous drugs, chemicals and medicinal substances the following: veronal, barbitol, acid diethylbarbituric, barbituric acid, or any of their salts, derivatives or compounds, phenobarbital, or any of its salts or compounds, acetylurea, sulfonated methanes, or any of their salts, derivatives or compounds. Once filled, prescriptions are not to be refilled without the written order of the prescriber, it was reported.

Housman Sentenced.—Dr. Nathan S. Housman, San Francisco, was sentenced to San Quentin prison, June 13, to a term of from one to fourteen years, after the court had denied a motion for a new trial. Housman was indicted by the grand jury, November 1, on six counts: two of perjury, two of preparing false evidence and two of offering false evidence. Shortly before his indictment, Dr. Housman had been acquitted in municipal court on two misdemeanor charges involving narcotic prescriptions, according to the state board of medical examiners. It was stated that testimony was given to prove that Dr. Housman perjured himself at the jury trial prior to the indictment when he said that he kept case records showing narcotic prescriptions issued to patients. Material from the state board of medical examiners states that the falsification charges were based on an allegation that Dr. Housman's case records showing narcotic prescriptions had been copied after the start of his trial from records of prescriptions kept at the drugstore at which the prescriptions were filled. Judge Lile T. Jacks imposed the sentence of from one to fourteen years on each of the two counts of perjury and of from one to five years on each of the other counts, all of the terms to run concurrently. Dr. Housman graduated at Jefferson Medical College of Philadelphia in 1922.

CONNECTICUT

Changes in Health Officers.—Dr. Howard S. Allen, Woodbury, has been appointed health officer of Bethlehem; Dr. Morton H. Chapnick of the town of Putnam and city of Putnam, and Dr. Francis Brae Rafferty, Willimantic, of Lebanon.

State Medical Election.—Dr. James D. Gold, Bridgeport, was named president-elect of the Connecticut State Medical Society at its annual meeting in Hartford, May 21, and Dr. Arthur B. Landry, Hartford, was inducted into the presidency. Dr. Creighton Barker, New Haven, was reelected secretary. The next annual session will be in Bridgeport, May 20-22, 1941.

Appointments at Yale.—Dr. John R. Paul and Leon S. Stone, Ph.D., both associate professors, have been appointed professor of preventive medicine and Bronson professor of comparative anatomy respectively at Yale University School of Medicine, New Haven. Dr. Paul graduated at Johns Hopkins University School of Medicine, Baltimore, in 1919 and has been on the Yale faculty since 1926. Dr. Stone received his doctorate at Yale in 1921. George H. Smith, Sc.D., professor of immunology, has been appointed assistant dean for the next college year.

IDAHO

Society News.—The South Side Medical Society was addressed in Twin Falls, May 17, by Drs. Fern M. Cole, Caldwell, president of the state medical association, who discussed the value of medical organization, and Casper W. Pond, Pocatello, deep infections of the neck.

Study of Silicosis.—A mobile x-ray unit, built by the state industrial accident board and state division of public health, is making a tour of the state under the direction of the bureau of industrial hygiene. All industrial workers exposed to silica dust will be examined. According to *Northwest Medicine*, the information will be used for statistical purposes only and it is not expected that the unit will be used to replace any existing medical service.

INDIANA

Course in Obstetrics.—The St. Joseph County Medical Society and the bureau of maternal and child health of the Indiana State Board of Health conducted a postgraduate course in obstetrics in South Bend, June 3-5. Sessions were held at Epworth and St. Joseph hospitals. The course was under the direction of Dr. Carl P. Huber, assistant professor of obstetrics, Indiana University School of Medicine, Indianapolis, and director of postgraduate education in obstetrics of the state board of health.

New Hospital Library.—The new \$8,000 library at the Indianapolis City Hospital was dedicated May 14. It was the gift of Eli Lilly & Co. A feature of the dedicatory program was the presentation of the first volume to the library by Dr. William N. Wishard Sr., superintendent of the hospital from 1879 to 1887. The book was the "Autobiography of Dr. Harvey Wiley." Dr. Wishard also presented photographs of Dr. Wiley and of Dr. Livingston Dunlap to the library. The latter is credited with founding the hospital. Dr. Charles W. Myers, now superintendent of the city hospital, presided at the dedicatory ceremonies.

Direction of Medical Schools Consolidated.—Dr. Willis D. Gatch, dean and professor of surgery, Indiana University School of Medicine, Indianapolis, has been appointed to direct the unit at Bloomington, newspapers announced June 22. In the latter capacity he succeeds Dr. Burton D. Myers, whose retirement was announced in *THE JOURNAL*, June 15. According to the report, the consolidation of direction will assure continuity of training at minimum cost and maximum effectiveness for students. Jacob A. Badertscher, Ph.D., professor of anatomy at Bloomington since 1921, will be assistant to Dr. Gatch in Indianapolis, and Dr. Edwin N. Kime, who has been a member of the faculty since his graduation from the school in 1916, will be in charge of the department of anatomy on both campuses, giving full time to the work. Dr. Badertscher holds Ph.D. degrees from Ohio and Cornell universities and the degree of Ph.M. from Ohio University, Athens, Ohio. After serving on the faculties of both of these schools he joined the Indiana faculty in 1914. Dr. Gatch has been professor of surgery at the university since 1911 and dean since 1931.

IOWA

State Medical Election.—Dr. Earl B. Bush, Ames, was chosen president-elect of the Iowa State Medical Society at its annual session in Des Moines, May 3, and Dr. Frank P. McNamara, Dubuque, was inducted into the presidency. Dr. Robert L. Parker, Des Moines, was reelected secretary. Davenport was designated as the place for the next annual session, May 14-16, 1941.

Society News.—Dr. Norbert C. Barwasser, Davenport, addressed the Muscatine County Medical Society, May 23, on "Management of the Commoner Skin Diseases."—Dr. Palmer Findley, Omaha, discussed "Socialized Medicine in Sweden" before the Des Moines Academy of Medicine and the Polk County Medical Society recently.—Dr. William D. Paul, Iowa City, discussed "Recent Advances in Hypertension" at a meeting of the Bremer County Medical Society and the staff of Mercy Hospital in Waverly recently.—The Hardin County Medical Society was addressed in Iowa Falls recently by Dr. Joseph B. Priestley, Des Moines, on "Nonsurgical Management of Gallbladder Disease."—Dr. Willard O. Thompson, Chicago, discussed "Treatment of Hypogonadism Pertinent to Endocrinology" before the Woodbury County Medical Society recently.—Dr. Elmer E. Kottke, Des Moines, addressed the Hancock-Winnebag County Medical Society recently on "Heart Disease and Coronary Hypertension."

KANSAS

State Medical Election.—Dr. Clyde D. Blake, Hays, was chosen president-elect of the Kansas Medical Society at its recent annual meeting in Wichita and Dr. Forrest L. Loveland, Topeka, was installed as president. Dr. John M. Porter, Concordia, is secretary, and Mr. Clarence G. Munns, Topeka, executive secretary. Topeka was selected as the place for the 1941 session.

MASSACHUSETTS

Conference on Tomorrow's Children.—The Harvard Summer School and the National Conference on Family Relations will sponsor a New England Conference on Tomorrow's Children at Littauer Center, Harvard University, Cambridge, July 24-26. The conference program will consist of panel and round table discussions. Among physicians who will take part at various times are:

Dr. John Rock, research associate in obstetrics and instructor of gynecology, Harvard Medical School, Boston.
Dr. Merrill Moore, associate in psychiatry, Harvard Medical School, Boston.
Dr. Florence Clothier, psychiatrist, New England Home for Little Wanderers, Boston.
Dr. James C. Janney, assistant professor of gynecology, Boston University School of Medicine.
Dr. Woodbridge E. Morris, New York, medical director, Birth Control Federation of America.
Dr. Anna L. Philbrook, New Hampshire State Hospital, Concord.
Dr. George Gilbert Smith, Boston, president, Massachusetts Society for Social Hygiene.
Dr. Regine J. K. Stix, Milbank Memorial Fund, New York.
Dr. Eric P. Stone, Providence, R. I., chairman, medical advisory board, Rhode Island Maternal Health Association.

New Society for Research in Psychiatry.—The Massachusetts Society for Research in Psychiatry was organized at a meeting, May 2, to stimulate research in psychiatric medicine and the sciences allied to it in the psychiatric institutions of the state. The active membership is limited to those who have completed or presented before a recognized scientific society, or published in a recognized scientific journal, results of research work which they have done within the last five years. This active membership will cease after more than three years has elapsed without production of original work, the member becoming an associate member. The associate members are selected from those having a satisfactory background and training which will render them suitably qualified to become research workers and from those who are participating in research work. Meetings will be held six times a year at the various hospitals engaged in neuropsychiatric work. They are to be devoted to symposiums and to informal discussions of projects, methods, techniques and demonstrations of research work actively engaged in or under consideration. Officers of the new society include Drs. William Malamud, Worcester, president; Paul I. Yakovlev, Waltham, vice president, and Kenneth J. Tillotson, Belmont, secretary-treasurer.

MICHIGAN

Personal.—Dr. Harry H. Haight, Crystal Falls, has been appointed superintendent of the Penn Iron Mining Company Hospital, Norway, to succeed Dr. Lloyd E. Hamlin, who resigned to become medical director of the plant of the Bethlehem Steel Corporation, Bethlehem, Pa., newspapers reported. —Dr. Charles M. Turrell, physician to the Detroit police department since 1914, has retired.—Dr. Frank H. Power, Ann Arbor, has been appointed by the governor as cancer consultant to the state department of health; in this capacity he will serve as field agent for the department and the cancer committee of the Michigan State Medical Society and will be available as a consultant to practicing physicians. He succeeds Dr. Clifford H. Keene, who resigned.—Dr. Stuart Pritchard, president and general director of the W. K. Kellogg Memorial Foundation, Battle Creek, received the honorary degree of doctor of science from the University of Michigan, Ann Arbor, June 15, for "distinguished and outstanding contributions to the field of medicine and public health."

MISSISSIPPI

State Medical Election and Meeting.—Dr. Augustus Street, Vicksburg, was named president-elect of the Mississippi State Medical Association at its seventy-third annual meeting in Jackson, May 16, and Dr. William H. Anderson, Booneville, was installed as president. Other officers are Drs. Charles E. Mullins, Bude; Martin L. Flynt Sr., Meridian, and William H. Curry, Eupora, vice presidents. Dr. Thomas M. Dye, Clarksdale, was reelected secretary. The 1941 session will be held in Biloxi, May 13-15. Dr. Irvin Abell, Louisville, Ky., gave

the Ewing Howard Fox Oration on "Some Contributions of the Profession to the Public." Included among other speakers were:

Dr. Edgar W. Davis, Washington, D. C., Lobectomy and Pneumonec-tomy in Nontuberculous Disease of the Lungs.
Dr. Edward C. Ellett, Memphis, Tenn., Some Points in Eye Surgery.
Dr. Alston Callahan, Vicksburg, Tumors of the Orbit.
Dr. John J. Shea, Memphis, Tenn., Frequent Errors in Tonsil and Adenoid Surgery.
Dr. William Lauch Hughes, Jackson, Diseases of the Nasopharynx.
Dr. Fred Geisenberger, Natchez, Modified Barraquer Suction Extraction of Cataracts.
Dr. Douglas D. Baugh, Columbus, Intercepting Cancer in the Female Reproductive Organs.
Dr. Robert Lyle Motley, Memphis, Tenn., Some Points in the Diagnosis and Treatment of Indigestion.
Dr. Charles E. Ward, Jackson, Treatment of Eczema in Children.
Dr. John G. Archer, Greenville, Some Observations of Bundle Branch Block.
Dr. Rudolph H. Kampmeier, Nashville, Tenn., Benign Tertiary Manifestations of Syphilis Presenting Difficulties in Diagnosis.
Dr. Aubrey V. Beacham, Magnolia, Systemic Effects of Frequently Overlooked Urinary Diseases.
Dr. Willard H. Parsons, Vicksburg, Indications for and Results from Operations on the Biliary Tract.
Dr. John C. Henthorne, Jackson, Pathologic Defections of the Corpus Luteum of the Ovary.
Dr. Hugh A. Gamble, Greenville, Breast Cancer, Its Treatment and the Cautery Technic of Operation.
Dr. Van Buren Philpot, Houston, Cesarean Section.

One of the features of the meeting was the presentation of a portrait of Dr. John Wesley Monette, 1803-1851, for Mississippi's first medical hall of fame. The presentation was made by Judge Gerald Brandon, Natchez, grandson of Dr. Monette.

NEW MEXICO

State Medical Election.—Dr. Carl Mulky, Albuquerque, was chosen president-elect of the New Mexico Medical Society at its fifty-eighth annual meeting and Dr. William B. Cantrell, Gallup, was installed as president. Drs. Wallace P. Martin, Clovis, and Leo B. Cohenour, Albuquerque, were reelected vice president and secretary-treasurer, respectively. Raton was selected as the place for the 1941 annual meeting.

NEW YORK

Personal.—The Delaware County Medical Society gave a reception May 21 to honor Dr. Robert Brittain, Downsville, on his completion of fifty years of medical practice.—Dr. John H. Korn, Olean, who has resigned as superintendent of Rocky Crest Sanatorium and director of tuberculosis work of Cattaraugus County, was honored with a testimonial dinner before his departure for Westchester County. About 200 friends of Dr. and Mrs. Korn attended and Dr. Theodore J. Holmlund, Cattaraugus, president of the Cattaraugus County Medical Society, presented them with a silver bowl, the gift of friends throughout the county. Dr. Korn became director of the division of tuberculosis in the Westchester County health department May 16.

Syracuse Alumni Meeting.—The medical alumni of Syracuse University School of Medicine, Syracuse, held a meeting in connection with commencement June 3-4. Dr. George H. Whipple, Rochester, was the guest speaker at an afternoon session on "Protein Construction and Exchange in the Body—Including Hemoglobin and Plasma Proteins," followed by section meetings on surgery, medicine, pediatrics and gynecology and obstetrics. Tuesday morning addresses were made by Drs. Jesse G. Marthens, Dayton, Ohio, and Leonard K. Stalker, Rochester, Minn., whose subjects were: "Can We Eliminate the Shadow on the Land?" and "Management of Acute Conditions Within the Abdomen" respectively. Dr. George Baclir, New York, was the guest speaker at the annual banquet Monday evening at the Onondaga Hotel.

New York City

Medal Awarded to Dr. Greene.—Dr. James Sonnett Greene, founder and director of the National Hospital for Speech Disorders, was awarded a medal by the American Laryngological, Rhinological and Otological Society at its meeting in New York, June 7, "for his unselfish devotion to the alleviation of speech defects in those thus afflicted, and for the success which has crowned his lifelong efforts in having established the National Hospital for Speech Disorders." A citation accompanied the medal, which is said to be the fourth awarded by the association in the forty-six years of its existence. Dr. Greene graduated at Cornell University Medical College, New York, in 1902.

Health and Teaching Centers Completed.—The Washington Heights Health and Teaching Center, last of a group of centers affiliated with the five medical schools in New York, was dedicated June 10. The new center adjoins the College

of Physicians and Surgeons of Columbia University, with which it is associated, on land made available by the Presbyterian Hospital. Mayor La Guardia made the principal address and other speakers included Drs. Nathan B. Van Etten, President of the American Medical Association; Willard C. Rappleye, dean and professor of medical economics of the College of Physicians and Surgeons, and John L. Rice, commissioner of health. The Lower East Side Health and Teaching Center, 341 East Twenty-Fifth Street, affiliated with New York University College of Medicine, was dedicated, May 15. The speakers included the mayor, Dr. Rice, Harry Woodburn Chase, LL.D., chancellor of New York University, which donated the land for the building; Dr. Currier McEwen, dean and associate professor of medicine, of New York University College of Medicine; Dr. Harry S. Mustard, Hermann M. Biggs professor of preventive medicine at the college, and John M. Schiff, president of the Henry Street Settlement, which will provide nursing services at the center. The new structure, adjoining the college of medicine, cost about \$375,000. Child health and dental clinics are on the first floor; tuberculosis and rheumatic cardiac services on the second; offices for health education and the Henry Street Visiting Nurse Service on the third floor; quarters for the district health officer and his staff on the fourth, and class rooms and laboratories of the department of preventive medicine of the college of medicine on the fifth and sixth floors. This teaching center is the fourth of the units the city has set up in cooperation with medical schools. Those opened previously are the Kips Bay-Yorkville center in cooperation with New York Hospital-Cornell University Medical College; East Harlem in cooperation with New York Medical College and Flower Hospital, and Red Hook-Gowanus in cooperation with Long Island College of Medicine.

NORTH CAROLINA

Dr. MacNider Resigns as Dean.—Dr. William deB. MacNider, dean of the University of North Carolina School of Medicine, Chapel Hill, since 1937, has resigned to continue his research activities as Kenan research professor of pharmacology. Dr. Walter Reece Berryhill, who has been assistant dean since 1937, has been made acting dean. Dr. MacNider graduated from the medical school of the university in 1903, became Kenan professor of pharmacology in 1905 and research professor in 1920.

Society Honors High Point Physician.—The Guilford County Medical Society gave a dinner recently in honor of Dr. David A. Stanton, High Point, who has practiced medicine for fifty-three years. Dr. Frederick R. Taylor paid tribute to Dr. Stanton as a physician and Mayor O. A. Kirkman lauded him as a citizen. The society presented to him an engraved scroll. Dr. Stanton graduated from Vanderbilt University School of Medicine, Nashville, in 1887 and has practiced in High Point since 1891. He has been mayor and health officer of the town, a member of the city council and of the board of education.

OKLAHOMA

Course in Obstetrics.—A new intramural postgraduate course for physicians in obstetrics and allied subjects was begun early in June under the auspices of the University of Oklahoma School of Medicine, Oklahoma City, in cooperation with the state department of health and the Children's Bureau of the U. S. Department of Labor, Washington, D. C. The course will be repeated intermittently as circumstances and demand may justify. In conjunction with the physicians' course, and with the same sponsor and cooperating agencies, the University of Oklahoma School of Nursing will offer a four month postgraduate course in obstetrics and related subjects.

Society News.—Dr. Tazwell D. Rowland, Shawnee, addressed the Pottawatomie County Medical Society, Shawnee, June 15, on "Mental Problems Met in General Practice."—The medical societies of Garfield, Kay, Noble, Payne and Pawnee counties held a joint meeting in Perry, June 20, with recreation in the afternoon and addresses in the evening by Dr. Henry H. Turner, Oklahoma City, president of the Oklahoma State Medical Association, on the problems of the association and Mr. Joseph Hamilton, executive secretary of the crippled children's commission, on phases of that work.—Dr. Forrest P. Baker, Talihina, addressed the Tulsa County Medical Society, Tulsa, May 27, on "Tuberculosis and Admissions to the State Hospital."

PENNSYLVANIA

District Meetings.—The Ninth Councilor District of the Medical Society of the State of Pennsylvania held a meeting in Punxsutawney, June 21. On the scientific program Dr. George E. Simpson, Indiana, presented a paper entitled "Stop and Go in Biliary Surgery"; Dr. Talcott Wainwright, Oil City, "Shock," and Dr. Frank A. Lorenzo, Punxsutawney, "A Message from the Committee on Industrial Health of the Medical Society of the State of Pennsylvania." Dr. Francis F. Borzell, Philadelphia, president-elect of the state society, discussed activities of the society and a fifty year certificate was presented to Dr. Thomas N. McKee, Kittanning.—Drs. Edward F. Burt and David W. Kramer, Philadelphia, addressed the Fourth Councilor District meeting at Berwick, June 20, on "Respiratory Infections of Children" and "Progress Report on Control of Diabetes" respectively. Drs. Charles H. Henninger, Pittsburgh, president, and Walter F. Donaldson, Pittsburgh, secretary of the state society, made addresses and a fifty year testimonial certificate was presented to Dr. John W. Bruner, Bloomsburg.

Pittsburgh

Syphilis Control.—A program for the control of syphilis was inaugurated in Pittsburgh June 12 under grants from the city, the state, the federal government and the Buhl Foundation, amounting to \$100,000. A general diagnostic clinic, to be coordinated with existing clinics, was opened at the Falk Clinic at the University of Pittsburgh, with Dr. William H. Guy as chief clinician, Dr. William W. Wightman as assistant chief clinician and twenty other physicians as part time clinicians. Six full time nurses are employed by the program and will be available to physicians for follow-up work. Dr. Albert E. Russell of the U. S. Public Health Service is temporary director of the program until it is under way, according to the *Pittsburgh Medical Bulletin*. Indigent patients will be treated at the clinics, but those able to pay will be referred to private physicians.

TEXAS

Special Society Elections.—Dr. Boen Swinny, San Antonio, was elected president of the Texas Allergy Association at its annual meeting, May 13, in Dallas, and Dr. Homer E. Prince, Houston, secretary.—Officers of the Texas Dermatological Society elected at the annual meeting, May 13, were Drs. William A. Smith, Beaumont, president; James Lewis Pipkin, San Antonio, vice president, and Duncan O. Poth, San Antonio, secretary.—Dr. William B. Carrell, Dallas, was made president of the Texas Orthopedic Association at its meeting, May 13; Dr. Edmund M. Cowart, Houston, vice president, and Dr. Mary Ruth Jackson, Dallas, secretary.—At the third annual meeting of the Texas Society of Gastro-Enterologists and Proctologists, May 13, officers elected were Drs. Milford O. Rouse, Dallas, president; Hugh C. Welsh, Houston, and Gilbert E. Brereton, Dallas, and Thomas E. Smith, Dallas, secretary.—Officers elected at the meeting of the Texas Association of Medical Anesthetists were Drs. Thomas H. Compere, Houston, president; Frank O. Barrett, El Paso, vice president, and Robert A. Miller, San Antonio, secretary.

VIRGINIA

Society News.—Dr. Ben M. Baker Jr., Baltimore, was the guest speaker at the annual all day clinic meeting of the Norfolk County Medical Society, Norfolk, recently on "The Therapeutic Use of Histamine." Clinics were held in the morning at the Norfolk General Hospital. Drs. Richard B. Nicholls and Charles J. Andrews addressed the society recently on "Obstetric Complications and Sterility" and "Management of the Third Stage of Labor, with Description of a New Technic for Delivery of the Placenta" respectively.—Drs. Byrd S. Leavell, Charlottesville, and William P. McGuire, Winchester, addressed the Medical Society of Northern Virginia in Winchester recently on "Acute Glomerulonephritis, Clinical Course and Treatment" and "Acute Oculoglandular Tularemia" respectively.—Theodore Blum, D.D.S., New York, addressed the annual joint meeting of the Peninsula Dental Society and the Warwick County Medical Association, recently in Newport on "Mouth Lesions: Their Diagnosis and Treatment."

Retires from State Service.—Dr. Bathurst B. Bagby, for several years director of the state bureau of child health, was to retire from service, July 1, newspapers reported. Dr. Bagby graduated at George Washington University School of Medicine, Washington, D. C., in 1904. He engaged in private prac-

tice until 1923, when he became health officer of Henrico County. In the following year he took a similar position in Clark County, Ga. He was health officer of Southampton County from 1929 to 1930, when he joined the staff of the state department of health. He was president of the Virginia Public Health Association in 1930.

WASHINGTON

Society News.—Dr. Wallace D. Hunt, Seattle, was elected president of the Washington Public Health Association at the annual meeting in Port Angeles, May 17-18.—Drs. Paul G. Flothow and Thomas W. Blake, Seattle, addressed the Cowlitz County Medical Society, Longview, May 15, on "Surgical Lesions of the Spine Causing Low Back Pain" and "Radiologic Aspects of Low Back Pain" respectively.—Dr. Alfred O. Adams, Spokane, addressed the Walla Walla Valley Medical Society, Walla Walla, May 9, on "Vitalium for Internal Fixation of Fractures."—Drs. Ross D. Wright and Charles P. Larson, Tacoma, addressed the Yakima County Medical Society, Yakima, May 13, on "Proctologic Surgery" and "Newer Knowledge of Vitamin K" respectively.

WEST VIRGINIA

Joint Meeting of State Societies.—The Medical Society of Virginia will hold its annual meeting jointly with the West Virginia State Medical Association, July 29-31, at the Greenbrier, White Sulphur Springs. General sessions will be held each morning and round table discussions each afternoon. The guest speakers will be:

Dr. Ralph M. Tyson, Philadelphia, Management of Urinary Infections in Childhood.
Dr. George E. Bennett, Baltimore, Orthopedic Treatment of Arthritis.
Dr. Carl M. Peterson, Chicago, The A. M. A. Bureau of Industrial Health.
Dr. Ross Golden, New York, Lesions of the Small Bowel.
Dr. Walter C. Alvarez, Rochester, Minn., The Patient Who Is Always Complaining.
Dr. Wesley C. Bowers, New York, Sinus Therapy.
Dr. Alfred I. Folsom, Dallas, Texas, The Female Bladder.
Dr. Harvey B. Stone, Baltimore, The Delayed Treatment of Appendicitis.
Dr. Karl M. Bowman, New York, Treatment of Delirium.
Dr. Frederick C. Irving, Boston, Treatment of Pernicious Vomiting.

Dr. Irvin Abell, Louisville, Ky., will deliver the oration on surgery and Dr. Paul Dudley White, Boston, the oration on medicine. Dr. Frank V. Langfitt, Clarksburg, president of the West Virginia association, and Dr. Hugh H. Trout, Roanoke, president of the Medical Society of Virginia, will deliver their official addresses Tuesday evening, July 30.

PUERTO RICO

Personal.—Dr. Cesar Dominguez, Humacao, has been reappointed a member of the Board of Medical Examiners of Puerto Rico.—Dr. Oscar G. Costa-Mandry, San Juan, president of the Puerto Rico Medical Association, has been made an honorary member of the Society of Physicians and Surgeons of Costa Rica.

GENERAL

Base Hospital Reunions.—The U. S. A. Base Hospital Camp Grant Reunion Association announces its annual reunion to be held in Milwaukee at the Y. M. C. A., Monday, September 16. Former medical officers, nurses and enlisted men of the Camp Grant Hospital are invited to attend this reunion. Reservations should be sent to Harold E. Giroux, president of the association, 841 Barry Avenue, Chicago.—Physicians who served at U. S. A. Base Hospital, Camp Sevier, Greenville, S. C., are requested to communicate with M. R. Callaway, 405 West Fourth Street, Dayton, Ohio, with regard to a reunion to be held in connection with the American Legion Convention in Boston, September 23-26.

Second Evaluation of Serologic Tests.—The Committee on Evaluation of Serodiagnostic Tests for Syphilis, in cooperation with the U. S. Public Health Service, is planning a study of serologic tests for syphilis or modifications of these within the next year similar to one conducted by the same committee in 1935. The methods used will be comparable to those used in the earlier study (*THE JOURNAL*, Dec. 1, 1934, p. 1705). If the need for an investigation of this kind seems to justify the cost, invitations will be extended to the authors of such serologic tests who live in the United States or who may be able to participate by the designation of a serologist who will represent them in this country. Serologists who have an original serologic test for syphilis or an original modification thereof and who desire to participate in the second evaluation study should submit their applications not later than October 1.

The applications must be accompanied by a complete description of the technic of the author's serologic test or modification. All correspondence should be directed to the Surgeon General, U. S. Public Health Service, Washington, D. C.

National Board Celebrates Anniversary.—The National Board of Medical Examiners celebrated the twenty-fifth anniversary of its founding at a dinner at the Waldorf-Astoria, New York, June 12. Major-Gen. Merritte W. Ireland, president of the board, presided at the dinner and the speakers were Dr. Alan Gregg, director of medical sciences, Rockefeller Foundation, "A Sponsor's Greeting"; the Rev. Alphonse M. Schwitalla, Ph.D., dean, St. Louis University School of Medicine, "The Medical Schools"; Dr. Robert W. Keeton, professor of medicine, University of Illinois College of Medicine, "The Diplomates and the Medical Profession," and Dr. Walter L. Bierring, Des Moines, Iowa, "The First Twenty-Five Years." The board, founded in 1915 by Dr. William L. Rodman, Philadelphia, has received support from six foundations: Carnegie Foundation for the Advancement of Teaching, Rockefeller Foundation, Commonwealth Fund, Milbank Memorial Fund, General Education Board and the Carnegie Corporation. Its certificate is now accepted by forty-three states, the territories of the United States and several foreign countries. It now has thirty-two members.

Physician's Kit and Instruments Found.—In reporting the apprehension of one Woodfin Holsapple as an illegal practitioner in Illinois, the assistant state's attorney at Rock Island announces the finding of a physician's kit and instruments. The bag, which was in Holsapple's possession when he was arrested, contained the prescription book of a physician in Colorado, who has since reported that the kit and instruments are not his. No details were reported concerning Holsapple's activities in Illinois, but the assistant state's attorney suggested that some effort be made to return the apparently new kit to its rightful owner. It is suggested that any physician who has lost a kit or instruments should write Mr. Sam M. Arndt, assistant state's attorney, Rock Island, Ill., giving a description of the missing articles. Whether or not the Holsapple mentioned above is the same person as Woodfin Holsapple who was found to be posing as a physician in Colorado in 1939 is not known. Subsequent investigation disclosed that the latter individual had never obtained a medical degree from any university and that he had never practiced (legally) medicine. The person in this case pleaded guilty and was sentenced to serve six months in the Denver County jail.

Special Society Elections.—Dr. Andrew C. Ivy, Chicago, was elected president of the American Gastro-Enterological Association at the annual meeting in Atlantic City, N. J., in June. Drs. Russell S. Boles, Philadelphia, and Sara M. Jordan, Boston, were elected vice presidents and Dr. Thomas T. Mackie, New York, was made secretary. The 1941 meeting will be held in Atlantic City at the Hotel Claridge, May 5-6.—Dr. Fred O. Butler, Eldridge, Calif., was chosen president-elect of the American Association on Mental Deficiency at its annual session in May and Meta L. Anderson Post, Ph.D., Newark, N. J., was inducted into the presidency. Dr. E. Arthur Whitney, Elwyn, Pa., was reelected secretary. The next annual meeting has been set tentatively for June 24-28, 1941, in Salt Lake City.—Dr. George M. Coates, Philadelphia, was chosen president of the American Otolological Society at its annual meeting May 27. Dr. Isidore Friesner, New York, is secretary. The 1941 meeting will be May 26-28 in Atlantic City, N. J.—Dr. Harold Douglas Singer, Chicago, was designated president-elect of the American Psychiatric Association at its annual meeting, May 24, and Dr. George H. Stevenson, London, Ont., was installed as president. Dr. Arthur H. Ruggles, Providence, was reelected secretary. The next annual session will be in Richmond, Va.—Dr. Harold D. Corbusier, Plainfield, N. J., was reelected president of the Academy of Physical Medicine at its annual meeting in Richmond, Va. Drs. Gervase J. P. Barger, Washington, D. C., and Thomas F. Wheeldon, Richmond, were elected vice presidents. The 1941 meeting will be in New York.

LATIN AMERICA

Society News.—The first Brazilian Congress of Gynecology and Obstetrics will be held in Rio de Janeiro, September 8-15. Subjects to be discussed are recent advances in gynecologic endocrinology, diagnosis and treatment of cervical cancer, endocrinology in obstetrics and the social aspect of obstetric care. Dr. Arnaldo de Moraes, Rio de Janeiro, is president of the organizing committee.—Drs. Federico Gómez and Luis Berlanga Berumen, Mexico City, have been elected president and secretary, respectively, of the Mexican Society of Pediatrics for 1940-1941.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 15, 1940.

Internment of Alien Physicians and Nurses

The organized treachery employed in the attacks on small countries now known as "fifth column" activities has led to extensive precautions in Britain. These include the internment of all enemy aliens between the ages of 16 and 60 and restrictions on other aliens. This regulation has caused serious inconvenience to alien physicians and students. At the present time many are studying medicine at the Edinburgh school. Of these a large proportion are of German or Austrian nationality, mostly refugees from persecution. But it is not possible to be sure that some enemy emissaries are not among them, masquerading as refugees. For the safety of the country all aliens of enemy nationality have therefore to be interned. Some hold house appointments in the hospitals. Their internment will therefore cause inconvenience to the hospitals as well as to themselves. Aliens who are not of enemy nationality are not interned but their movements are restricted, as possibly they also may include dangerous elements. There are many American undergraduates at Edinburgh who are prohibited by the regulation from being outdoors after 8 p. m. At the medical school about fifty are working. Representations are being made on their behalf for some relaxation of the curfew. One of the grounds is that their freedom of movement at night is necessary for attendance at emergency work in the hospital. Twenty-nine sisters and nurses of the German Hospital, London, have been interned, following a visit of the police.

Second Removal of Children

The removal from London and other centers to places of greater safety from air raids of 1,270,000 persons in four days was described in *THE JOURNAL* May 25, page 2134. Of these nearly 1,000,000 were children. The evacuation was entirely voluntary but was strongly advised by the government and arranged by it in every detail. But many parents did not avail themselves of the scheme and about 800,000 children remained. As the expected air attacks did not materialize, many children were brought back to their homes. The approach of the war to our shores has caused the government to arrange a second evacuation of children. About 120,000 are now being removed from London, and the process is to be completed in a week. They are going west, the majority to Cornwall, Devon, Somerset and Wales, where they will be far from the areas considered dangerous. But it is estimated that there are still in London 300,000 children whose parents are unimpressed by the government appeals to register them for evacuation.

Wounded Brought From France to England

The emergency hospital scheme created for the care of civilian casualties and the great majority of military casualties is now receiving its first adequate test. During the past two weeks there have been received from France thousands of military casualties which have been distributed over fifty hospitals in Britain. In the House of Commons, the minister of health, Mr. Malcolm MacDonald, stated that the reception and care of the men from the battle line had worked smoothly and satisfactorily. French and other allied wounded who have been evacuated from Dunkirk have also arrived in England. In a broadcast an eminent surgeon, who, as usual in such cases, remains anonymous, assures the public that the wounded are having the best care that can be provided by a service which includes almost all the best brains in the medical profession.

Physical Therapy for War Injuries

Attention has been called in the press by surgeons and others to the need for adequate and early facilities for the physical-therapeutic treatment in hospitals of war injuries. On behalf of the Ministry of Health Sir George Chrystal, secretary, received a deputation of the Health and Housing Committee of the House of Commons, who came to emphasize this need. In reply Sir George Chrystal said that the ministry regarded it as essential that the scheme for the treatment of orthopedic and war strain injuries should provide for physical therapy not only in the early but in the recovery or convalescent stages. Patients with other types of injury would receive any necessary further treatment of this kind, either as outpatients at hospitals or from general practitioners. With regard to cases occurring in the armed forces, the ministry was planning their treatment with the War Office. At all the general hospitals in the Emergency Medical Service, massage and electrical treatment at the bedside were available. There were also nineteen special orthopedic centers at which massage, radiant heat, electrical treatment and remedial exercises would be available. At these centers there would be also departments for occupational treatment. The service provided five centers for war strain in addition to the effort syndrome center in London. Here remedial exercises and remedial occupations were being provided. These twenty-four centers were in different parts of the country. The intention was to transfer to them from the general hospitals all cases which required their special facilities. The ministry was now reviewing the hospitals with a view to ensuring that the necessary apparatus was available wherever necessary. The deputation expressed itself as satisfied that the ministry was bringing the standards in the emergency hospital scheme up to a high level.

Laurence O'Shaughnessy Killed in the War

One of the most brilliant of the younger surgeons, Mr. Laurence O'Shaughnessy, the thoracic surgeon, has been killed in Flanders while serving as a major in the Royal Army Medical Corps. He was only 39. He qualified F.R.C.S. at the age of 23. In 1924 he was appointed medical inspector in the Sudan, where he stayed for seven years. During this period he visited Sauerbruch's clinic and so became interested in thoracic surgery. He left the Sudan and spent six months with Sauerbruch and then obtained the Royal College of Surgeons research fellowship, which enabled him to do experimental work to the Downe research farm. In 1933 as Hunterian professor he lectured at the college on the surgery of the esophagus and two years later on the surgery of the root of the lung. He published a paper on traumatic shock which is considered classic. When the London county council, with the encouragement of Lord Dawson, formed a clinic at the Lambeth Hospital for the surgical treatment of cardiovascular disease, he was appointed consultant surgeon. He was also thoracic surgeon to the city of Birmingham tuberculosis scheme and various sanatoriums for tuberculosis. He did much work on the surgical treatment of tuberculosis and introduced the operation of thoracotomy. But it is for his work on the surgery of the heart, culminating in his operation of cardio-omental anastomosis, that he is best known. After much experimental work he introduced this operation to provide a collateral circulation in cases of cardiac ischemia with its resultant angina pectoris. In 1938 he was able to report twenty cases in which he had performed the operation. Those who survived the operation for one year, and in some cases for two years, at the time of the report continued to be active. The operation is of course a severe one for patients already debilitated by disease, and the general view is that its value still remains to be assessed. He published about thirty papers and wrote the section on the esophagus and diaphragm in Maingot's *Post-Graduate Surgery*. In 1937 he collaborated with Sauerbruch in a book on thoracic

surgery. He also collaborated with Kayne and Pagel in their book on pulmonary tuberculosis. It is a tragic irony that this man, who did so much to give credit to Germany for the surgery of the chest, should have died by German hands and from a wound in the chest.

SWITZERLAND

(From Our Regular Correspondent)

May 28, 1940.

Prevention of War Epidemics

Dr. Hermann Mooser, professor of hygiene, recently addressed the medical society of Zurich on the prophylactic measures employed at the present time against war epidemics. Mooser has had a wide experience in tropical regions and recently was in charge of a hygienic mission sent to China by the League of Nations. He pointed out that military forces fed under hygienic conditions may develop diseases of the digestive tract the infective agent of some of which had not yet been isolated. Intestinal inflammations of this kind do not last more than from twenty-four to forty-eight hours, are traceable to colds and have a benign evolution. In poisoning by meat caused by *Salmonella enteritidis*, *Bacillus brucellensis* and *Salmonella suipestifer*, partly due to intoxication, partly to infection, animal paratyphosis is involved. New infections arise from this source. Infection by contact is infrequent. Carriers and excretors of bacilli are exceptional. Army physicians need to bear in mind that meats do not show signs of infection and that vegetables and pastry may also be at fault, if meat remnants, bouillon and so on are used in their preparation. Medical science is yet insufficiently informed about essential epidemiologic aspects of bacillary dysentery, in contrast with our knowledge regarding typhus infection, paratyphus infection and infection due to meat poisoning. At any rate the infectiousness of dysentery compared with that of other gastrointestinal diseases is exceedingly high. Mooser indicated that even in China it was more difficult to combat dysentery than cholera and typhus. The statistics of the World War showed that vaccinations against typhus and paratyphus greatly increased prophylaxis against epidemics. No doubt could any longer be entertained of the value of subcutaneous immunization against abdominal typhus and paratyphus; however, statistics on the efficacy of peroral immunization were still far from univocal. Prophylactic immunization against diphtheria has not been possible yet because of the variety of infectious agents and the intense local reactions. On the other hand, diseases of the respiratory tract are much more difficult to control. There is, however, an exceedingly great divergence between the number of infected and the number of manifestly ill persons. This is true not only for poliomyelitis but for cerebrospinal meningitis, designated by Mooser as a rare complication of infection of the nasopharyngeal passage due to meningococci. In poliomyelitis a fourteen day quarantine of the affected military force is the appropriate measure; in epidemic meningitis care must be added. Fatigue is known to create to a high degree a predisposition to the disease. Young recruits, unaccustomed to military strain and stress, are much more susceptible than soldiers in the regular service.

Anti Air Raid Hospital Planned

In consequence of the war, the erection of a large bomb proof hospital offering protection against air raids and capable of resisting the severest bombardments has been decided on in Basel, a city bordering on the German and French frontiers. Four entrances are planned to provide access and to meet the hazard of partial obstruction by debris. The equipment also is planned to meet the needs of battles on a large scale. Degassing of gassed persons is calculated to require, on the average, eight minutes. This will make possible the degassing of 3,000 persons daily. About 500 slightly wounded persons could be taken care of daily on a twenty-four hour working

schedule and 100 operations of seriously wounded performed, with possible blood transfusions, in three planned operating rooms. The cost of construction is estimated at 800,000 Swiss francs (about \$180,000).

Additional War Measures

All physically fit Swiss men have been called to the colors. However, they receive temporary furloughs and are subject to emergency recall. These regulations apply more or less also to the medical profession. Since the outbreak of the war, Swiss physicians have divided their time between their company and their private practice. Arrangements have been made for university students to continue their studies. Students required to take examinations in the spring were given furloughs. Other students receive furloughs good for two months. This enabled them to complete about half of a semester and was credited to them for a full semester's work. The Swiss federal government has also ordered special examination periods for medical students in preparation of the gaps caused by the mobilization of the medical profession. The practical half year required of all medical students has likewise been canceled for the duration of the war and two years following.

The section on war hygiene formerly belonging to the division of war welfare within the federal department of economics has been transferred to the federal health department. It is charged with hygienic problems that affect the welfare of the civilian population because of the military surveillance of the country's borders. It cooperates closely with the sanitary division of the army and with the sanitary service division (*grenz-sanitätsdienst*) operating on the borders. This last named division exercises health control jurisdiction over all persons entering Switzerland. Those suspected of an infectious disease are assigned for observation to certain hospitals within the border area. Similarly, persons attacked by a noninfectious disease are turned over by this federal agency to civilian hospitals.

The medical societies of Berne, Zurich and other cities largely concern themselves with problems arising from the war. Necessary sanitary measures are taken everywhere and pertinent discussions prepared. For example, the medical society of Geneva prepared a training course on war medicine and surgery. This course lasted a month and was conducted by specialists for Swiss army physicians, nearly all of whom are civilian practitioners. Prof. René Leriche, French surgeon of Strasbourg, was one of the lecturers.

Marriages

JAMES WILLIAM FOUCHE, Columbia, S. C., to Miss Lease Wyman of Greenwood in Aiken, June 8.

ROBERT HAL GINGLES, Oklahoma City, to Miss Helen Louise Wilson of Chickasha, Okla., May 30.

ALFRED STENGEL JR., Philadelphia, to Miss Anne Adelle Hammett of Chestnut Hill, Pa., June 15.

MARCUS KELLOGG MOOKERJEE to Miss Marie Louise Borchart, both of Milwaukee, May 4.

SAMUEL STUART DU PUY, Beckley, W. Va., to Miss Helen E. Baker of Morgantown, June 1.

MAX S. KRAUS, Rockaway Beach, N. Y., to Miss Caroline Gottlieb of New York, May 26.

JULIUS L. BOIARSKY, Charleston, W. Va., to Miss Hortense Marguerite Balacaier, April 14.

EUNICE LE BARON STOCKWELL to Mr. Walter Baker, both of Philadelphia, June 15.

WILLIAM HENRY LANE JR. to Miss Jane Zimmer, both of Indianapolis, May 25.

SAMUEL NIEDER, Gilman, Ill., to Miss Myrtle Levinson of Chicago, May 26.

Deaths

Calvin Brewster Coulter, Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1913; associate professor of pathology at the Long Island College of Medicine; associate in bacteriology at his alma mater, 1923-1924, associate professor of bacteriology from 1924 to 1934 and later associate professor of sanitary science; member of the American Society for Experimental Pathology; served during the World War; served at various times and in various capacities on the staffs of the Kings County Hospital, Long Island College Hospital, Nassau Hospital, Mineola, N. Y., Brooklyn Hospital and the Prospect Heights Hospital; aged 52; died, May 10, in the North Country Community Hospital, Glen Cove, N. Y., of pneumonia.

Bertram Lewis Bryant ♂ Bangor, Maine; Medical School of Maine, Portland, 1898; member of the House of Delegates of the American Medical Association from 1920 to 1923, from 1925 to 1928 and from 1930 to 1933; formerly secretary of the Maine Medical Association; past president of the Penobscot County Medical Association; consulting physician to the Waldo County Hospital, Belfast, and the Bangor State Hospital; medical director of the Bangor Sanatorium; aged 67; pathologist from 1899 to 1903, visiting physician from 1903 to 1934 and consulting physician since 1934 at the Eastern Maine General Hospital, where he died, May 10, of uremia.

William Albert Henke ♂ La Crosse, Wis.; Illinois Medical College, Chicago, 1906; University of Illinois College of Medicine, Chicago, 1913; past president of the Wisconsin Hospital Association and the La Crosse County Medical Society; for many years chairman of the county board of health; aged 59; medical director of the Grandview Hospital, where he died, May 8, of coronary sclerosis.

Donald St. Clair Campbell, La Plata, Md.; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1916; member of the Medical and Chirurgical Faculty of Maryland; deputy state health officer for Charles County; served during the World War; aged 46; died, May 15, in the Georgetown University Hospital, Washington, D. C., of hemorrhage due to esophageal varix.

John David Moore ♂ Bloomfield, N. J.; Yale University School of Medicine, New Haven, Conn., 1902; member of the American Academy of Ophthalmology and Otolaryngology; attending surgeon at the Newark Eye and Ear Infirmary, Mountainside Hospital, Montclair, and the Essex County Hospital for Contagious Diseases, Belleville; aged 64; died, May 12.

John Aloysius Sanders, Omaha; John A. Creighton Medical College, Omaha, 1911; for many years assistant in clinical obstetrics at his alma mater and instructor in anatomy in the dental school; on the staffs of the Nicholas Senn Hospital, St. Catherine's Hospital and St. Joseph Hospital; aged 55; died, May 23, in Sioux Falls, S. D., of carcinoma of the rectum.

Bernard W. Hays, Jackson, Mo.; University of Louisville (Ky.) Medical Department, 1894; University and Bellevue Hospital Medical College, New York, 1899; member and past president of the Missouri State Medical Association; on the staffs of St. Francis and Southeast Missouri hospitals, Cape Girardeau; aged 72; died, April 18, of coronary disease.

E. Weldon Young ♂ Seattle; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1889; fellow of the American College of Surgeons; on the staffs of the Maynard Hospital, Columbus Hospital, Swedish Hospital and the King County Hospital; aged 70; died, May 9, of hypertensive cardiovascular disease.

John Calvin Wright, Antigo, Wis.; Rush Medical College, Chicago, 1882; member of the State Medical Society of Wisconsin; formerly county physician, city physician and health officer; at one time secretary of the Langlade County Medical Society; aged 82; on the staff of the Langlade County Memorial Hospital, where he died, May 11.

Walter Otts Allen, Hendersonville, N. C.; Medical College of the State of South Carolina, Charleston, 1926; member of the Medical Society of the State of North Carolina; served during the World War; aged 42; died, May 13, in the Johns Hopkins Hospital, Baltimore, of petrositis and pneumococcal meningitis.

Len Lenton Culp ♂ Des Moines, Iowa; University and Bellevue Hospital Medical College, New York, 1889; Illinois Medical College, Chicago, 1900; formerly special physician at large for the Indian Service; member of the Indiana State Medical Association; died, May 10, of coronary thrombosis.

Logan B. Zintsmaster, Massillon, Ohio; Western Reserve University Medical Department, Cleveland, 1901; member of the Ohio State Medical Association; fellow of the American College of Surgeons; served during the World War; on the staff of the Massillon City Hospital; aged 63; died, May 10.

Hyman Israel Vener ♂ Los Angeles; University of Illinois College of Medicine, Chicago, 1925; assistant clinical professor of medicine, University of Southern California School of Medicine; member of the city health department; aged 49; died, May 23, in Cedars of Lebanon Hospital of uremia.

Clarence Sylvester Cook, Los Angeles; Chicago College of Medicine and Surgery, 1910; member of the California Medical Association; served during the World War; on the staffs of the Methodist Hospital, Queen of Angels Hospital and the French Hospital; aged 53; died, May 8.

Horace Clifford Stroup, Seward, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1925; served during the World War; on the staff of the Lee Homeopathic Hospital, Johnstown; member of the board of health of Seward; aged 43; died, May 5, of carcinoma of the rectum.

John Henry Weber, Akron, Ohio; Western Reserve University Medical Department, Cleveland, 1902; member of the Ohio State Medical Association; fellow of the American College of Surgeons; surgeon to the City Hospital; aged 62; died, May 13, of cerebral hemorrhage.

Morris Lee King, New Canaan, Conn.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1881; formerly medical director of the New York Life Insurance Company; aged 83; died, May 13, of cerebral hemorrhage and arteriosclerosis.

Harry Garfield Wright, De Kalb, Ill.; Hahnemann Medical College and Hospital, Chicago, 1907; at one time county coroner; formerly state senator; served during the World War; aged 58; died, April 17, in Holland, Pa., of heart disease, diabetes mellitus and kidney stones.

Max Emmert ♂ Omaha; Johns Hopkins University School of Medicine, Baltimore, 1909; fellow of the American College of Surgeons; surgeon to the Nebraska Methodist Episcopal Hospital; aged 56; died, May 16, in the Immanuel Hospital of coronary thrombosis.

Irving Darche ♂ Brooklyn; University and Bellevue Hospital Medical College, New York, 1928; assistant physician on the staff of the Beth-El Hospital; aged 38; died, May 17, in the Jewish Hospital of nasopharyngeal carcinoma with metastasis to the brain.

Albert W. Lewis Jr., Atlanta, Ga.; University of Tennessee College of Medicine, Memphis, 1932; member of the Medical Association of Georgia; assistant in pharmacology and in medicine at the Emory University School of Medicine; aged 29; died, May 13.

Hubert Sidney Smith, Thibodaux, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1898; member of the Louisiana State Medical Society; director of the Lafourche Parish Health Unit; aged 75; died, May 2, of coronary thrombosis.

Lincoln C. Chenoweth ♂ Joplin, Mo.; Missouri Medical College, St. Louis, 1886; an Affiliate Fellow of the American Medical Association; past president of the Jasper County Medical Society; aged 75; on the staff of St. John's Hospital, where he died, May 5.

William Baker Furman, Eastley, S. C.; Medical College of the State of South Carolina, Charleston, 1908; member of the South Carolina Medical Association; county health officer; past president of the Pickens County Medical Society; aged 56; died, May 21.

Francis Edward Morgan, Santa Cruz, Calif.; University of California Medical Department, San Francisco, 1881; formerly county coroner, county physician, county and city health officer; aged 83; died, April 30, of chronic myocarditis and bronchiectasis.

James A. Christian, Dardanelle, Ark.; Kansas City College of Medicine and Surgery, Kansas City, Mo., 1921; formerly member of the state legislature; aged 44; died, May 2, in a hospital at Little Rock of coronary occlusion and ruptured appendix.

Morris Buist Garner, Madison, Tenn.; College of Physicians and Surgeons, Memphis, 1907; formerly a lawyer; member of the Tennessee State Medical Association; past president of the Middle Tennessee Medical Association; aged 61; died, May 11.

Patrick Francis Moylan, Scranton, Pa.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1890; member of the Medical Society of the State of Pennsylvania; aged 76; died, May 30, of carcinoma of the stomach.

Albert Milo Shattuck, Worcester, Mass.; Dartmouth Medical School, Hanover, N. H., 1895; member of the Massachusetts Medical Society; on the staffs of the Worcester City and the Memorial Hospital; aged 69; died, May 26, of arteriosclerosis.

Albert Joseph Vesely, Creve Coeur, Ill.; University of Illinois College of Medicine, Chicago, 1934; member of the Illinois State Medical Society; aged 32; was killed, May 18, when the automobile in which he was driving was struck by a train.

William Harland Emery, Coatesville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1896; aged 70; died, May 3, in the Chester County Hospital, West Chester, of myocardial degeneration and cirrhosis of the liver.

Thomas Melville Talbot, Falls Church, Va.; University of Maryland School of Medicine, Baltimore, 1870; member of the Medical Society of Virginia; aged 91; died, May 3, of fracture of the neck of the femur and bronchopneumonia.

William LeRoy Marks @ Pittsburgh; University of Pennsylvania School of Medicine, Philadelphia, 1911; resident physician at Carnegie Institute of Technology; aged 55; died, May 23, in the Presbyterian Hospital of coronary thrombosis.

Milan Coburn, Coopersville, Mich.; Detroit College of Medicine, 1893; member of the Michigan State Medical Society; for many years health officer; aged 81; died, May 25, in Grand Rapids of coronary sclerosis and cardiac decompensation.

Nan Gilbert Seymour @ New York; Cornell University Medical College, New York, 1902; medical director of the William Booth Memorial Hospital; aged 64; died, May 27, of lobar pneumonia, type III, and bilateral psoas abscess.

Howard Alfred Bayles, Port Chester, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1901; member of the Medical Society of the State of New York; aged 62; died, May 20, of metastatic carcinoma.

Wayne Neal Freemyer @ Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1912; served during the World War; aged 56; died, May 30, in St. Vincent's Infirmary of nephrolithiasis with abscess and embolus.

Benjamin F. Shamblin, Lyerly, Ga.; Atlanta Medical College, 1888; member of the Medical Association of Georgia; aged 80; past president of the Chattooga County Medical Society; died, May 20, of carcinoma of the rectum.

Burnham Roswell Benner, Lowell, Mass.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1875; member of the Massachusetts Medical Society; aged 93; died, May 29, of arteriosclerosis.

Robert M. McCreight, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1887; for many years police surgeon; aged 78; died, May 17, in St. Joseph's Hospital of hypertensive cardiovascular disease.

Cecil Claude Bowie, Carroll, Iowa; State University of Iowa College of Medicine, Iowa City, 1907; member of the Iowa State Medical Society; on the staff of St. Anthony Hospital; aged 59; died, May 24, of toxemia.

Fred Melvin Cole @ Gardiner, Maine; College of Physicians and Surgeons, Boston, 1908; school physician; formerly health officer; on the staff of the Gardiner General Hospital; aged 61; died, May 5, of acute coronary thrombosis.

Adolph Steiner, Cleveland; University of Wooster Medical Department, Cleveland, 1891; for many years on the staff of the Mount Sinai Hospital; aged 72; died, May 16, of carcinoma of the sigmoid with metastasis to the liver.

Frank Ellis Estes, Compton, Calif.; Denver and Gross College of Medicine, 1904; veteran of the Spanish-American and World wars; for many years district health officer; aged 63; died, April 29, of coronary arteriosclerosis.

Benjamin H. Bainbridge, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1895; aged 71; died, May 29, in the Philadelphia General Hospital of bronchopneumonia and arteriosclerotic heart disease.

Edward Laurence Patterson, Fayetteville, Ark.; Atlanta (Ga.) School of Medicine, 1908; served during the World War; on the staff of the Veterans Administration Facility; aged 55; died, May 22 of coronary thrombosis.

Henry Edward Bittner, Hazleton, Pa.; Jefferson Medical College of Philadelphia, 1902; for many years member of the city board of education; aged 70; died, May 25, of arteriosclerosis and cerebral hemorrhage.

Theodore Francis Trimble, Corpus Christi, Texas; University of Rochester School of Medicine, 1932; member of the State Medical Association of Texas; aged 36; was killed, May 5, in an automobile accident.

Louis Howard Wilmot, Ansonia, Conn.; University of the City of New York Medical Department, 1891; city health officer; for many years on the staff of the Griffin Hospital, Derby; aged 70; died, April 23.

George A. Stanton, Belding, Mich.; St. Louis College of Physicians and Surgeons, 1893; past president of the Ionia County Medical Society; aged 82; died, April 21, in the Presbyterian Hospital, Los Angeles.

John Alexander Dales @ Sioux City, Iowa; Rush Medical College, Chicago, 1890; fellow of the American College of Surgeons; on the staff of the Methodist Hospital; aged 79; died, May 13, of heart disease.

Hunter Robb Sunkle, Cleveland; University of Cincinnati College of Medicine, 1929; member of the Ohio State Medical Association; on the staff of the Lutheran Hospital; aged 36; died, May 15, of myocarditis.

Robert Arthur Haggard, Arcola, Miss.; Atlanta School of Medicine, 1912; member of the Mississippi State Medical Association; served during the World War; aged 56; died, May 15, of angina pectoris.

J. W. Wyman, Denmark, S. C.; University of Georgia Medical Department, Augusta, 1893; member of the South Carolina Medical Association; aged 67; died, May 1, in Columbia of cholelithiasis.

George W. Holt, Malabar, Fla.; University of Tennessee Medical Department, Nashville, 1901; veteran of the Spanish-American War; aged 61; died, May 11, of cerebral hemorrhage and chronic myocarditis.

Sanford W. Forbush, Beloit, Wis.; Northwestern University Medical School, Chicago, 1907; member of the State Medical Society of Wisconsin; aged 56; died, May 18, of coronary thrombosis.

William Sandusky @ Seward, Neb.; John A. Creighton Medical College, Omaha, 1910; past president of the Seward County Medical Society; owner of the Seward Hospital; aged 59; died, April 28.

Malaku Emmanuel Bayen, New York; Howard University College of Medicine, Washington, D. C., 1935; aged 40; died, May 4, in the Rockland State Hospital, Orangeburg, N. Y., of lobar pneumonia.

Irving Masten Vanderhoff @ Newark, N. J.; University and Bellevue Hospital Medical College, New York, 1905; on the staff of the Presbyterian Hospital; aged 58; died, May 2, of heart disease.

John McQuirk Leonard, Blairsville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1903; served during the World War; aged 61; died, May 21, of chronic pyelonephritis.

Emma Hammond Wheeler, New Bedford, Mass.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1893; aged 80; died, May 24, in Fairhaven of cerebral thrombosis.

I. Phillip Pollack, Hempstead, N. Y.; New York University College of Medicine, 1939; intern at the Meadowbrook Hospital; aged 24; died, April 21, of hemolytic streptococcus meningitis.

John Langland Lundby, Irwin, Iowa; Northwestern University Medical School, Chicago, 1910; member of the Iowa State Medical Society; aged 56; died, May 30, of coronary occlusion.

George Franklin Harding, Brookline, Mass.; Harvard Medical School, Boston, 1889; member of the Massachusetts Medical Society; aged 77; died in May of carcinoma of the prostate.

Francis Marion Frazier, Bryan, Ohio; Fort Wayne (Ind.) College of Medicine, 1891; also a lawyer; formerly judge of the court of common pleas in Williams County; aged 82; died, April 26.

George William Roland Bowie, Vanceboro, Maine; Jefferson Medical College of Philadelphia, 1934; member of the Maine Medical Association; aged 30; died in May of tuberculosis.

Jordan E. Ruhl, Kansas City, Mo.; Central Medical College of St. Joseph, Mo., 1903; Barnes Medical College, St. Louis, 1904; aged 71; died, May 30, of carcinoma of the prostate.

Ross B. Cobb, Philadelphia; University of Maryland School of Medicine, Baltimore, 1913; aged 69; died, May 19, in the Atlantic City (N. J.) Hospital of chronic myocarditis.

Robert Newton Pitts, Memphis, Tenn.; Atlanta Medical College, 1890; veteran of the Spanish-American War; aged 74; died, May 20, of coronary thrombosis and cardiorenal disease.

Howard Lewis Pintler ☉ Peoria, Ill.; Hahnemann Medical College and Hospital, Chicago, 1901; aged 65; died, May 25, in St. Francis Hospital of diffuse fibrinopurulent peritonitis.

George Brookins, Caroga Lake, N. Y.; Albany (N. Y.) Medical College, 1894; aged 72; died, May 20, in the Montgomery Sanatorium, Amsterdam, of pulmonary tuberculosis.

Bernard Harrington Taylor ☉ Marion, Ohio; St. Louis University School of Medicine, 1928; on the staff of the Marion City Hospital; aged 37; died, May 9, of angina pectoris.

Frank Smith Jennings, St. Petersburg, Fla.; University of the City of New York Medical Department, 1880; member of the Florida Medical Association; aged 81; died, May 9.

Wilton Daniel Garrett, West Winfield, N. Y.; University of the City of New York Medical Department, 1885; aged 83; died, April 8, of chronic nephritis and arteriosclerosis.

Linton Williams Struble, Davenport, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1897; aged 73; died, May 12, of coronary thrombosis.

William Ernest Long ☉ Pearland, Texas; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; aged 60; died, May 14.

Arthur Robert Higdon, Fancy Farm, Ky.; Hospital College of Medicine, Louisville, 1901; member of the Kentucky State Medical Association; aged 61; died, May 12.

George E. Willoughby, Gosport, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1905; aged 71; died, May 8, of coronary occlusion and arteriosclerosis.

Elmer John Austin ☉ Fort Steilacoom, Wash.; University of Oregon Medical School, Portland, 1934; on the staff of the Western State Hospital; aged 47; died, April 29.

Ransom Joseph Parker ☉ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1893; aged 70; died, May 3.

William Barrett Acker, Hannibal, N. Y.; Bellevue Hospital Medical College, New York, 1894; health officer; aged 70; died, May 7, of coronary thrombosis.

Henry Vernon Logan, Miami Beach, Fla.; Medical College of Indiana, Indianapolis, 1897; served during the World War; aged 67; died, May 22, of myocarditis.

Quintus L. Shelton, Loneoak, Ky.; University of Tennessee Medical Department, Nashville, 1899; aged 73; died, May 23, of uremia due to hypertrophy of the prostate.

William Cook Martin, Kansas City, Mo.; Eclectic Medical University, Kansas City, 1912; aged 69; died, May 18, in Sabetha, Kan., of hemorrhagic nephritis.

Ernest Arnold Guyton, Eau Claire, Wis.; Saginaw (Mich.) Valley Medical College, 1900; aged 75; died, May 13, in the Luther Hospital of bronchopneumonia.

William Brehon Nash, Stanton, Tenn.; Vanderbilt University School of Medicine, Nashville, 1915; served during the World War; aged 48; died, April 30.

Audly Theodore Rank, Van Wert, Ohio; Eclectic Medical Institute, Cincinnati, 1906; member of the Ohio State Medical Association; aged 61; died, April 25.

Nathaniel J. Ridley, Lexington, Ky.; Meharry Medical College, Nashville, Tenn., 1900; aged 73; died, May 23, of carcinoma of the abdominal viscera.

Arthur Denman Van Dyke ☉ Scranton, Pa.; University of the City of New York Medical Department, 1883; aged 80; died, May 4, of coronary sclerosis.

Martha Rau Williams, Cincinnati; Laura Memorial Woman's Medical College, Cincinnati, 1897; aged 76; died, May 24, of chronic myocarditis.

Samuel B. Steele, Hot Springs National Park, Ark.; Louisville (Ky.) Medical College, 1894; aged 70; died, May 4, of chronic nephritis and uremia.

Arthur R. Wilson, Milwaukee; College of Physicians and Surgeons of Chicago, 1886; aged 83; died, May 8, of myocarditis and pernicious anemia.

Avery Leroy Myrick, Daytona Beach, Fla.; University of Alabama School of Medicine, 1910; aged 55; died, May 21, of hypertensive heart disease.

Benjamin F. McNeil, Des Moines, Iowa; University of Illinois College of Medicine, Chicago, 1902; aged 68; died, May 14, of arteriosclerosis.

Benjamin Hoff Searing, Newburgh, N. Y.; Cornell University Medical College, New York, 1903; aged 61; died, April 15, at St. Luke's Hospital.

Winfield Holmes Miller, Reno, Nevada; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1920; aged 43; died, May 16.

Whitfield Brooks Bean, Marianna, Ark.; Tulane University of Louisiana School of Medicine, New Orleans, 1894; aged 71; died, April 29.

Edgar J. Foote, Clarence, N. Y.; University of Buffalo School of Medicine, 1885; aged 80; died, May 1, in Buffalo of chronic myocarditis.

Thomas Jackson Hickman, Lenoir City, Tenn.; Tennessee Medical College, Knoxville, 1900; aged 80; died, May 8, in a hospital at Knoxville.

Charles Louis Weisberg, New York; University and Bellevue Hospital Medical College, New York, 1921; aged 42; died, April 30.

Lewis Nathaniel Foote, New York; New York University Medical College, New York, 1897; aged 67; died, May 6, of heart disease.

Thomas Davidson Macdonald, Central Valley, N. Y.; College of Physicians and Surgeons, Baltimore, 1904; aged 59; died in April.

Charles Sumner Laughlin, Vineland, N. J.; University of the City of New York Medical Department, 1878; aged 86; died in April.

Hugh N. Macdonald, Whycocomagh, N. S., Canada; Queen's University Faculty of Medicine, Kingston, Ont., 1882; died in May.

Theodore M. Wittkamp, Cincinnati; Cincinnati College of Medicine and Surgery, 1875; aged 86; died, May 21, of cerebral hemorrhage.

James William Nash ☉ Buffalo; Niagara University Medical Department, Buffalo, 1894; aged 68; died, May 5, of coronary occlusion.

Clarence Ernest Pickett, Richland, Ga.; Atlanta Medical College, 1894; served during the World War; aged 69; died, April 26.

Eliphaz Cowan Forbes, Ardmore, Tenn.; University of Nashville (Tenn.) Medical Department, 1899; aged 73; died, April 13.

Lillian Garabrant Perry, Hingham, Mass.; New York Medical College and Hospital for Women, 1896; aged 70; died, April 11.

John Valanglingham Mott, Amelia, Ohio; American Eclectic Medical College, Cincinnati, 1885; aged 76; died, May 17.

Alfred Clinton Smith, Lanett, Ala.; Atlanta School of Medicine, 1912; served during the World War; aged 53; died, May 18.

Walter Fairfield Thomison, Dayton, Tenn.; Vanderbilt University School of Medicine, Nashville, 1892; aged 80; died, May 5.

Thomas Arlander Martin, Loraine, Texas; Vanderbilt University School of Medicine, Nashville, 1892; aged 73; died, May 4.

Walter Wilson Thompson, Niagara Falls, Ont., Canada; Trinity Medical College, Toronto, 1889; aged 72; died, April 25.

Thomas Stephen Hession, Peoria, Ill.; College of Physicians and Surgeons, Keokuk, Iowa, 1891; aged 70; died, May 14.

Thomas J. Haines, Three Rivers, Mich.; College of Physicians and Surgeons of Chicago, 1888; aged 86; died, May 22.

John Alexander Sandbach, Irvington, Ky.; Hospital College of Medicine, Louisville, 1904; aged 65; died, May 2.

Alfred Thompson, Vancouver, B. C., Canada; Halifax (N. S.) Medical College, 1898; aged 70; died, April 20.

John Douglas Berry, Willowdale, Ont., Canada; Trinity Medical College, Toronto, 1890; aged 77; died, May 1.

Arthur George Hubbard ☉ Detroit; Maryland Medical College, Baltimore, 1900; aged 74; died, May 1.

A. Victory Seymour, Grosse Ile, Mich.; Detroit Homeopathic College, 1906; aged 55; died, May 28.

Bureau of Investigation

J. R. BREWSTER AND THE GOVERNMENT AGENCIES

His "Cures" Declared Fraudulent Again and Again by
Post Office Department, While Food and Drug
Administration also Objects (Unsuccess-
fully) and Federal Trade Commis-
sion Enters Complaint

Constant vigilance on the part of the Post Office Department is required to prevent individuals or companies whose fraudulent schemes have been debarred from the mails from continuing their businesses by operating under new names.

J. R. (Reese) Brewster and the Brewster Laboratories of Nashville, Tenn., conducted a mail order business in the sale of various nostrums which they falsely represented to cure tuberculosis, cancer, asthma and some other diseases. On Dec. 21, 1934, the Post Office issued a fraud order closing the mails to Brewster and his concern. Later, when it was discovered that Brewster was evading the order by continuing his fraudulent enterprise but using a new trade style, "New Deal Clinic," the original fraud order was extended to cover this name.

Again Brewster dodged! With Clyde Morris, said to be a relative, he was found to be running the same old fraud under still another name, "Dr. Reese Brewster." An inquiry addressed to that name brought the reply that the preparations supplied were the same as those sold for the previous fifteen years. The memorandum on the case reported that Morris admitted to the Post Office inspector that he was aware of the fact that fraud orders already had been issued against the scheme but that both he and Brewster intended to continue operating it unless stopped by conviction under the criminal statutes. Accordingly on Sept. 6, 1939, a supplemental fraud order was issued against the name Dr. Reese Brewster.

In an earlier case another government agency, the Food and Drug Administration, had seized interstate shipments of four nostrums sent out by J. R. Brewster when he was trading as Brewster Laboratories. Government chemists reported that the "Germ Destroyer" (for tuberculosis, cancer, asthma and some other things) contained a light petroleum oil, a saponifiable oil and turpentine; and that the three others were essentially similar in composition except that the "Throat Wash" (for tonsillitis and chronic throat trouble) also contained a trace of ferric chloride, the "Throat-Eaz" (for coughs, croup and "female trouble") included a trace of potassium iodide, and the "Liver Tonic" (for stomach disorders) contained no turpentine.

The government charged that the claims made for these products in the respective disorders named were fraudulent, but a jury in a district federal court brought in a verdict of not guilty.

In 1938 a third government agency, the Federal Trade Commission, also proceeded against what was apparently the same concern but at that time operating from Dallas, Texas. A release issued in September of that year reported that the Commission had entered a complaint against one Jefferson R. Brewster, who traded as Brewster Laboratories and Dr. Reese Brewster, charging misrepresentations in the sale of various nostrums. Among these were that "Brewster's G-D" is a protection against tuberculosis, a remedy for asthma, a relief of pain in any part of the body and, in combination with "Brewster's Tonic," a remedy for cancer; that "Brewster's T-Z" is a means of preventing or alleviating coughing spells and tubercular hemorrhages; that "Brewster's Sinine" is a treatment for sinus, mastoid, antrum, nose or ear trouble; that "Brewster's Pain Kill" is a treatment for rheumatism, neuritis and neuralgia and a cure for pneumonia and diphtheria; and that certain other Brewster preparations, not named, are treatments for kidney and stomach troubles, gallstones and goiter.

It was further charged that Brewster's products were not, as represented, prepared in laboratories nor had Brewster had

medical training or laboratory experience and consequently was not qualified to practice medicine. Apparently this case has not yet been settled.

Just why the Food and Drug Administration was unable to prove Brewster's claims fraudulent in the eyes of the jurors whereas the Post Office was later able to issue a fraud order is not clear. At least it is reasonable to presume that the Federal Trade Commission was justified in entering a complaint charging misrepresentations in the sale of Brewster's nostrums.

Correspondence

DETERMINATION OF PROTHROMBIN

To the Editor:—From the literature and from our correspondence with many American investigators it seems that there have been several investigators who have had difficulty in understanding certain details in our method for the determination of prothrombin. As a number of methods have been suggested for this purpose, it might interest American investigators working on coagulation of human blood to hear about our experiences in this field.

It is now generally agreed that the methods usually employed so far in the clinic for determination of the coagulation time and bleeding time are not accurate enough for examination of avitaminosis K and that the prothrombin has to be determined, i. e. that primarily the plasma has to be obtained without any admixture of tissue extract, and then the prothrombin in this plasma is determined by examining its coagulation on addition of tissue extract. Methods that do not follow this principle are too inaccurate and unspecific to be serviceable for further investigation of the significance of vitamin K or for the daily work in the clinic.

In the preparation of prothrombin-free plasma it is essential, of course, to prevent spontaneous coagulation of the blood—for instance by addition of an anticoagulant. For this purpose Quick uses oxalate and subsequent recalcination simultaneous with the addition of tissue extract. We have found, however, that greater accuracy is obtained by using heparin. When heparin is used it is not necessary to add calcium. An amount of 0.03 mg. of pure heparin to 4 cc. of blood is sufficient to prevent spontaneous coagulation of the blood without preventing coagulation on addition of thrombokinase (tissue extract) when this substance is added in larger amounts than are normally present in the blood (platelets). Thus the influence of the number of platelets is eliminated. The greatest advantage from the use of heparin, however, is that one can choose the quantity of heparin such that the measured coagulation times will range, for example, from two to six minutes, while with most other methods one has to measure coagulation times of a magnitude of about ten seconds for normal blood, which may be done only with essentially greater inaccuracy. Here it is further to be mentioned that with our modification of the heparin method some very interesting information can be obtained about anomalies of the coagulation in a number of other disorders (e. g. hemophilia). This information about the qualitative and quantitative aspects of the anomalies of coagulation mentioned will contribute to elucidate the nature of these diseases—data that might not be obtainable with other methods for examination of the coagulation.

The coagulation anomaly in avitaminosis K is a diminution in the ability of the blood to coagulate on addition of tissue extract, i. e. that addition of a certain amount of tissue extract to a given amount of blood gives a longer coagulation time for the diseased blood than for the normal. The proportion between the two coagulation times is a direct expression for the coagulation anomaly. The lowered capacity for coagula-

tion with tissue extract may also be expressed in this way: that a greater amount of tissue extract—for instance, R times as much—has to be added to a certain amount of K avitaminotic plasma than to the same amount of normal plasma in order to make it coagulate within a certain length of time, say three minutes. Then the value R is a direct expression for the coagulation anomaly; and it is in this way that we have defined the coagulation anomaly in our studies. Many investigators have preferred, however, to reckon with the prothrombin content of the blood instead of with the "R value." It will be appropriate, therefore, to point out that the effective prothrombin content of the blood can be found also by means of the R value method. This is done by diluting normal plasma with plasma free from prothrombin (for example, plasma treated with aluminum hydroxide). On determination of the R value for a series of such dilutions, it is easy to find the prothrombin concentration giving the same R value as the plasma in question.

Now it turns out that the R value is approximately reversely proportional to the prothrombin content, so that an R value of X corresponds to $100:X$ per cent of the normal prothrombin content. Thus analyses after the R value method are easily comparable to examinations giving the prothrombin content in percentage of normal. It is most rational, of course, to give the prothrombin content. So far we have preferred to express the coagulation anomaly by means of R values, partly because this means a direct expression for the coagulation anomaly but also because the coagulation of the blood is a far more complicated process, where the plasma exerts its influence on the coagulation time through many factors besides the prothrombin concentration. Here we have in mind the plasma component that is absent in hemophilia.

As to the value of determining the coagulation in clinical work after the principles outlined here, we think that it is essential always to keep in mind the great rapidity with which a fall in prothrombin may set in; this may occur also after an operation has been performed. It is to be emphasized that vitamin K therapy is to be instituted in every instance of obstructive jaundice even if there is no demonstrable decrease in prothrombin. So the significance of prothrombin determinations is merely that a decreased prothrombin is a warning against an operation, whereas normal values do not mean that the risk of fatal hemorrhage is excluded, unless a suitable vitamin K therapy is given.

Lately we have not published any data concerning the therapeutic aspects of the problem because Dr. Tage-Hansen, who has undertaken the clinical investigations, is going to publish a fairly comprehensive work on this subject. On account of the sudden great interest taken in the subject, he recently prepared a preliminary report of his studies, which was published in *THE JOURNAL*, Nov. 18, 1939, page 1875.

While it is true that ingestion of the vitamin together with bile salts acts more rapidly than intramuscular injections of emulsions, the main result of Tage-Hansen's work is that each of the three forms of administration has its particular advantages. Ingestion of vitamin K together with bile salts allows the use of rather crude vitamin K preparations but has the possible disadvantage of introducing extra bile salts into the organism. Intramuscular injection makes it possible to supply the organism with a store of vitamin K that is not absorbed so rapidly but the action of which lasts for weeks. Here oil may be used for the solutions. Intravenous injection of suitable emulsions has a very rapid effect, and it is possible by this method of introduction to use a smaller quantity than by ingestion.

HENRIK DAM.

JOHANNES GLAVIND.

Biochemical Institute, Copenhagen, Denmark.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SULFANILAMIDE THERAPY AND GRANULOCYTOPENIA

To the Editor:—Perhaps a year ago, and prior and subsequent to that time articles were published in *The Journal* concerning the complications of sulfanilamide therapy, particularly in reference to granulocytopenia and hemolytic anemia. Is it not true that granulocytopenia is apt to appear later than the first week of therapy and anemia during the first week? If a white count during therapy is 5,000 or less, should sulfanilamide always be promptly stopped? If the count is found to be between 1,500 and 2,000 can one always expect granulocytopenia to develop—that is, after the patients have been on sulfanilamide and there are no other diseases present to account for the leukopenia? If sulfanilamide is stopped before granulocytopenia develops but after leukopenia is present, is there still danger of the former developing? How long before the danger is over? Is anemia likely to develop after therapy has been stopped?
M.D., Iowa.

ANSWER.—In considering the changes which may occur in the blood of patients who are receiving sulfanilamide or its derivatives, it has been noted that acute hemolytic anemia generally occurs during the first five days of therapy, although one instance of this toxic manifestation has been reported on the twentieth day (Nelson, Edna L., and Scott-Young, Margery: *M. J. Australia* 1:629 [April 2] 1938). Slowly developing hemolytic anemia may occur at any time during the course of treatment with these drugs. Acute leukopenia with granulocytopenia, while most frequently seen during the first ten days of treatment, may be seen at almost any time during a course. These acute leukopenias are rarely accompanied by angina and are characterized by the fact that the polymorphonuclear leukocytes do not as a rule disappear completely from the peripheral blood. In many clinics it is a rule that if the granulocytes drop below 50 per cent of the differential count in adults, or below 40 per cent in children, therapy with sulfanilamide or its derivatives should be stopped. It is also wise to check carefully the differential white blood cell count when the total white blood cell count drops below 5,000.

It does not always follow that with the development of low total white blood cell counts, i. e. from 1,500 to 2,000 cells, one should necessarily expect granulocytopenia accompanied by angina and the other severe symptoms of this blood dyscrasia. Almost all of the actual cases of granulocytopenia which have been reported as occurring in the course of therapy with sulfanilamide and its derivatives have appeared after the fourteenth day of treatment, with the seventeenth to twenty-fifth days of therapy being the most common time for the development of this toxic manifestation. If such a leukopenia is noted and sulfanilamide is stopped before the granulocytes disappear, in most instances the granulocytes continue to decrease and granulocytopenia with angina develops. When a leukopenia with granulocytopenia has been noted in the course of treatment with sulfanilamide or its derivatives and the drug has been stopped, if an increase in the polymorphonuclear leukocytes does not occur within thirty-six hours it is highly probable that a true granulocytopenia is developing. The period of granulocytopenia in these patients may last from one to seven days before a return of polymorphonuclear leukocytes is noted.

If an acutely developing anemia is not present at the time at which therapy with sulfanilamide or its derivatives has been discontinued, there is little chance of an acute hemolytic anemia developing. However, if it has been noted that an acute hemolytic anemia is developing and sulfanilamide is stopped because of this toxic manifestation, the anemia generally continues to progress for two or three days despite the fact that the drug has been stopped.

HUMAN TUBERCULOSIS IN CATTLE

To the Editor:—Has there been any epidemiologic work done to show the amount of human tuberculosis in cattle and the hazard to cattle from farm employees with open tuberculosis?
M.D., New York.

ANSWER.—Typing studies on the infecting organism in bovine tuberculosis show that it is regularly the bovine type of tubercle bacillus. Repeated experimentation has shown that the human type bacillus is of low infectivity for cattle. In almost all type patients with open pulmonary tuberculosis in this country the infection is with the human type of tubercle bacillus. It seems

unlikely that a patient with this type of infection could infect cattle. T. G. Hull (Diseases Transmitted from Animals to Man, Springfield, Ill., C. C. Thomas, 1930) writes that "the human type of bacillus has never been found to infect cattle spontaneously." In other countries, however, where bovine tuberculosis is common, occasional cases of open pulmonary tuberculosis in man, due to infection with the bovine type of tubercle bacillus, occur. A. S. Griffith and W. T. Monro (The Relative Incidence of the Human and Bovine Types of Tubercle Bacilli in Human Tuberculosis in Scotland, *J. Path. & Bact.* 35:271 [March] 1932) wrote that the infecting organism in open respiratory tuberculosis was bovine in type in 3.8 per cent of 548 cases in Scotland. It is possible that caretakers expectorating the bovine type tubercle bacilli may infect cattle.

Although it is generally agreed that infection with human type tubercle bacilli does not cause significant lesions in cattle, there is evidence that it may sensitize them to tuberculin. Apparently massive infection is required. A. B. Cravford (*J. Am. Vet. M. A.* 89:562 [Nov.] 1936) found that about half of a group of bovine animals fed heavy doses of human type tubercle bacilli in sputum subsequently became tuberculin positive. The animals becoming allergic were not the ones receiving the heaviest dosage, but the dosage was large in all cases. Unless the feeding of bacilli was continued, sensitivity tended to disappear in a few months. At necropsy tuberculous lesions were not found. It has been reported from Finland (Stenius, R.: *Vet. Rec.* 50:633, 1938) that in a certain herd attended by a tuberculous patient a large percentage of the cows reacted to tuberculin. After the death of the attendant, the percentage of reactors decreased rapidly without removal of cattle from the herd. Three years after the attendant's death, no cattle in the herd reacted to tuberculin. No lesions were found in these cattle, although an acid-fast bacillus considered to be a human type tubercle bacillus was isolated from the tissues of one reactor. Whether such cases as the latter are to be considered conclusive or not, in view of the proof that sensitivity may be induced by tubercle bacilli experimentally it appears possible that the sputum of a patient with open tuberculosis, carelessly discharged in the food of cattle, might make them sensitive to tuberculin, at least transiently.

TOXIC ADENOMA AND DIABETES

To the Editor:—A white man aged 29, married, who is working in one of the local industrial plants, came to my office on Dec. 7, 1939, with the complaint of being 10 pounds under his usual weight. Except for nervousness, he had no other complaints. The blood pressure was 130 systolic, 80 diastolic, the pulse 92 per minute, the heart regular in rate, rhythm and force, the weight 128 pounds (58 Kg.) the thyroid enlarged, and there was a palpable adenoma of the right lobe and isthmus. The heart was synchronous with the pulse rate and there were no adventitious sounds. There was slight tenderness over the cecum and lower portion of the descending colon. Urinalysis showed 1 per cent of sugar present. December 14 the basal metabolism, determined at the local hospital, was +38. The fasting blood sugar was 185 mg. Because of the high basal rate I prescribed an organic iodine preparation. On Jan. 11, 1940, the urine was sugar free but the fasting blood sugar was 175 mg. On February 19 the basal metabolism was +38 per cent. He weighed 131 pounds (59 Kg.) the blood pressure was 120/80 and the pulse 68. There was no evidence of thyrotoxic symptoms. The urine was negative for sugar. On February 27 a sugar tolerance test revealed: fasting specimen, 188 mg.; one-half hour after taking dextrose, 208 mg.; one hour after taking dextrose, 204 mg.; two hours after taking dextrose, 179 mg.; three hours after taking dextrose, 185 mg.; four hours after taking dextrose, 188 mg. Could this be hyperglycemia due to an increased activity of the thyroid gland or could it be possible that both diabetes mellitus and an overactive thyroid exist without manifestations of thyrotoxicosis? If there is any literature that you can refer to on this matter, I shall appreciate it.

M.D., Pennsylvania.

ANSWER.—Glycosuria and hyperglycemia may occur in the presence of hyperthyroidism. In some instances this may reflect the influence of the increased metabolism. In others, particularly following the giving of dextrose, it may represent the tendency recently pointed out by Althausen, Lockhart and Soley (A New Diagnostic Test [Galactose] for Thyroid Disease, *Am. J. M. Sc.* 199:342 [March] 1940), who have demonstrated that in hyperthyroidism there is an increased rate of absorption of dextrose from the gastrointestinal tract. Blood sugar values above normal are obtained when dextrose is given orally and not when given intravenously.

Despite these considerations, in the case under discussion a diagnosis of diabetes mellitus is justified because the fasting blood sugars were 175 and 188 mg. per hundred cubic centimeters and even after the administration of dextrose the four hour value was still equal to that before the dextrose was administered.

The two basal metabolic rates, each plus 38 per cent, in addition to a palpable adenoma, suggest thyrotoxicosis, and it seems as though removal of the adenoma should lessen the severity of the diabetes somewhat but not eradicate it.

LATENT INFECTIONS

To the Editor:—A white man aged 69 fell acutely ill with fever, chills, nausea, vomiting and headache. He was first seen about two hours later. At first a relevant past history was not obtained. Examination revealed temperature 101.6, pulse 92, respirations 24, blood pressure 140/75. The head and neck were normal, the lungs clear to percussion and auscultation, the heart one fingerbreadth enlarged to the left. A slight systolic murmur over the apex in the sixth left interspace, and perpetual arrhythmia were noted. The abdomen was normal. There was a small area of erythema over the right lower tibia. The white blood count was 17,400 with 75 per cent polymorphonuclears. The urine was normal except for the sediment, which was loaded with pus cells and after being stained showed the presence predominantly of gram-positive cocci resembling staphylococci. Urinary symptoms were not complained of by the patient. On rectal examination the prostate was not enlarged, was not tender and showed no evidence of tumor or abscess. Within twenty-four hours there developed a cellulitis of the right lower leg with the classic signs of pain, swelling and redness. Lymphangitis proximal to the knee was not present but the vessels of the extremity between the ankle and knee joints were palpable and appeared indurated. The tibia was tender to pressure in its entire length. At this time the following additional history was obtained, after a small, innocent looking, slightly atrophic scar had been found over the midportion of the right tibia: Two months prior to the onset of the acute illness the patient injured his right leg by striking it against the sharp edge of his working table in the factory where he is employed. This resulted in a superficial abrasion requiring only self treatment by cleansing the wound with witch hazel. Uneventful healing occurred within a few days, leaving the scar described. In the light of these occurrences a provisional diagnosis of cellulitis and (metastatic?) urinary tract infection was made. Under sulfanilamide therapy and symptomatic measures the temperature fell to normal, the urine cleared and the cellulitis slowly resolved. X-ray examination two weeks after the onset of the acute illness showed no bone involvement, ruling out osteomyelitis. Except for a slight, noninflammatory, residual edema the patient completely recovered. A final diagnosis conforming to the provisional one was made. Blood cultures had not been taken because under the sulfanilamide therapy which was instituted at once no further chill or excessive rise in temperature occurred. The questions arise whether the minor injury to the right leg, having occurred two months previous to the development of cellulitis of the same extremity, can be considered a causative factor, in which case the patient would be entitled to workmen's compensation benefits. The patient's illness resembled septicemia, but (a) would it be possible for an infection to remain dormant for two months before causing the clinical picture described? (b) Can the original injury be regarded as contributing to it not solely causing the patient's illness (locus minoris resistentiae)? (c) If both questions are to be answered in the negative, what other etiology for cellulitis plus (metastatic) urinary tract infection would have to be considered in this case? (d) Are any similar cases on record? If so, please advise where I can find references.

M.D., New York.

ANSWER.—The case as described is complex and may be regarded from several points of view: 1. The abrasion may indeed have been a port of entry for an infection which later caused cellulitis and metastatic infection of the urinary tract. Latent infections of various kinds are known to exist for months or years, but in the case in question it seems unlikely that the trauma to the leg is important. The lesion was apparently superficial and healed promptly.

2. Infections anywhere in the urinary tract are not uncommon in a man 69 years old, particularly if obstruction is present, but no evidence of obstruction appears in the data given. When urinary tract infection is present, thrombophlebitis with cellulitis of the leg may complicate the picture as a secondary process, either as a metastatic localization during bacteremia or as the result of the abnormal rapidity of blood clotting with thrombus formation as an after-effect of infection.

3. If the vessels of the leg were palpable and indurated as mentioned, it is possible that latent thrombophlebitis may have been the source of a metastatic infection somewhere in the urinary tract, but not necessarily related to local trauma two months previously. If more careful bacteriologic studies had been made and the same kind of bacteria had been present in the two lesions, a relationship might be assumed with more assurance. For the same reason one cannot give credit to sulfanilamide for a cure in this case.

4. It is possible that the transient infection in the urinary tract and the cellulitis of the leg may both have been metastatic localizations of a blood borne infection arising elsewhere in the body.

To answer the questions raised, (a) it would be possible for infection to lie dormant, but improbable in this case according to the circumstances mentioned. (b) It is unlikely that the minor injury to the leg played any part in the condition described. (c) Already answered. (d) No cases of this sort have been found in the literature. Both conditions are so common as to make special reports unnecessary.

FREQUENCY OF SPINA BIFIDA

To the Editor:—I should like to have some information on the frequency of occurrence of spina bifida. I have examined several textbooks without finding any figures.

M.D., Illinois.

ANSWER.—Grinker's Neurology states that spina bifida occurs in 0.1 per cent of children; defects of closure of the various arches occur in the following proportion: cervical region 9.5 per cent, thoracic region 4.5 per cent, lumbar region 34 per cent, lumbosacral region 24 per cent and sacral region 23 per cent.

Woltman has stated that spina bifida is responsible for a sixth of the monstrosities encountered (Woltman, H. W.: Spina Bifida: A Review of 187 Cases, Including Three Associated Cases of Myelodysplasia Without Demonstrable Bony Defect, *Minnesota Med.* 4:244 [April] 1921).

Spina bifida occulta exists unrecognized in many instances throughout life and may or may not cause symptoms. Spina bifida occurs most frequently in the lumbar and sacral regions. No doubt the incidence of spina bifida varies considerably in the type of practice encountered.

DERMATITIS FROM CHEMICALS IN WATER

To the Editor:—Several miners, who have been working in a wet place underground, have developed severe dermatitis. The analysis of the water is as follows:

Total solids, nonvolatile.....	23.546	Gm. per liter
Total solids, as sulfates.....	29.406	Gm. per liter
Bicarbonate, HCO_3	0.0610	Gm. per liter
Bromide, Br.....	0.3572	Gm. per liter
Chloride, Cl.....	14.937	Gm. per liter
Sulfate, SO_4	0.2229	Gm. per liter
Silica, SiO_2	Trace	
Iron and alumina Fe_2O_3 and Al_2O_3	0.0280	Gm. per liter
Calcium, Ca.....	6.2324	Gm. per liter
Magnesium, Mg.....	0.6177	Gm. per liter
Sodium, Na.....	1.5632	Gm. per liter

These are probably combined as:

Sodium chloride, NaCl.....	4.099	Gm. per liter
Magnesium chloride, MgCl_2	2.419	Gm. per liter
Calcium chloride, CaCl_2	16.761	Gm. per liter
Calcium bromide, CaBr_2	0.447	Gm. per liter
Calcium bicarbonate, $\text{Ca}(\text{HCO}_3)_2$	0.081	Gm. per liter
Calcium sulfate, CaSO_4	0.353	Gm. per liter
Ferrie sulfate, $\text{Fe}_2(\text{SO}_4)_3$	0.070	Gm. per liter

What would cause the burns and what local treatment would be advisable?

M.D., Michigan.

ANSWER.—The dermatitis may be caused by one or all three of the following chemicals: magnesium chloride, calcium chloride and calcium bromide. Magnesium chloride partially decomposes in the presence of water into hydrochloric acid and magnesium oxychloride. Calcium chloride is a dehydrator, and calcium bromide decomposes under the action of carbon dioxide into hydrobromic acid and this on oxidation into free bromine.

Patch testing with the concentration of these chemicals found in the water may disclose which of them are the irritants. If it does not, a patch test with all three combined may show that it is their combined action on the skin which is causing the dermatitis.

Local treatment consists in removing the patient from his work and applying soothing applications such as boric acid solution or calamine lotion in the exudative stage, and boric acid ointment or Lassar's paste when the lesions are dry. Prevention consists in wearing waterproof coveralls or clothing and daily change to fresh work clothes.

SYMPTOMS AFTER REMOVAL OF NARCOTIC ADDICTION

To the Editor:—A woman aged 45 was a year ago completely removed from morphine, to which she had been addicted for nearly ten years. Late in her addiction she had taken as much as 25 grains (1.6 Gm.) daily by hypodermic injection. During the year since the withdrawal of the drug she has complained of severe pain in both shoulder joints, extreme nervousness, anorexia, insomnia and weakness. Careful study does not uncover any lesions to account for her symptoms. X-ray examination does not show any bone changes in the shoulder joints although motion apparently is painful. What are the usual effects on a patient who has for years taken large daily doses of morphine but who is finally cured of the addiction? Does the drug bring about any permanent pathologic changes when used for long periods?

M.D., Iowa.

ANSWER.—The habitual use of any narcotic produces a moral, mental and often physical deterioration, the latter chiefly due to a lack of proper nutrition, bad sanitation and irregular habits. Morphinism is not so much a disease in and of itself as chronic alcoholism, which produces a demonstrable pathologic change. Persons who have once had an addiction are prone to believe that any mental or physical stress that they have needs quick narcotic relief and are often unwilling or think they are unable to carry on without the quick relief and comfort that narcotics give. Asthenia, insomnia and nervousness

with pain or distress in different locations are common complaints of addicts after denarcotization. The fact that this patient used as much as 25 grains of morphine a day proves that she belongs to the type of individual with but little will power. There is no real physical need of an addict taking more than 8 or 10 grains (0.6 Gm.) of morphine a day. The excess does not give any real relief but often produces toxic symptoms.

RHEUMATIC FEVER AND PHYSICAL ACTIVITY

To the Editor:—About six months ago I took care of a case of acute rheumatic fever in a girl 10 years of age. The onset simulated infantile paralysis, there being apparent inability to use the lower limbs, some neck rigidity and high fever. The spinal fluid, however, was normal. The sedimentation rate at the onset was 35 mm. in one hour. After four weeks in bed the rate became normal. She was kept in bed another two weeks. No murmur was heard at any time. There was reduplication of the second sound in the third interspace, left, during the febrile stage. What is the modern tendency with regard to exercise and athletics in a child who seems to have an intact heart and is in good health otherwise? Is it wise to permit hand ball, basketball, tennis, swimming and all restrictions in this respect removed?

M.D., Wisconsin.

ANSWER.—The answer to this question is given without reference to the diagnosis of rheumatic fever in this particular case, for an insufficient amount of information is given for one to be certain of this diagnosis. The onset and short course of the disease are rarely encountered in children with rheumatic fever.

As a general rule, children with rheumatic fever have clinical or laboratory evidence of active disease for a few months at least. Rest is generally accepted as being wise as long as any evidence of infection persists. After active rheumatic fever subsides, a gradual increase in physical activity is the usual procedure. In a child without heart disease and no clinical or laboratory evidence of active rheumatic fever there is little evidence that any type of exercise is harmful to the patient. A recurrence of rheumatic fever is the possibility to be feared, and this is often associated with respiratory infection. Exercise apparently plays little or no part in such recurrences of the disease.

GAS COOKING RANGE FOR DRY STERILIZATION

To the Editor:—In the home in obstetric cases I use a small sterile pack which contains four towels, one small sheet, a cap, a gown and a mask. It is necessary to return these to my hospital many miles away for resterilization after they have been used. We have in our home a modern gas cooking range with an oven which has a dial heat control mechanism which starts in as low as 250 F. Could I use this dry heat for resterilization of these obstetric packs? What temperature should be used? For what length of time should it be used and would it destroy the fabric of the materials in the pack? Of course the materials are all cotton. All articles of the pack are simply covered with a muslin binder pinned well.

Bruce I. Ryder, M.D., Henry, Ill.

ANSWER.—There is no better method of sterilization than by dry heat for those objects which are not injured by it, such as clean glassware, clean bandages or towels, and even petrolatum. The temperature required is about 320 F. (160 C.) for a period of two hours. The packs should not be larger than necessary and should not be closely crowded in the oven. It may be that white cotton goods will become slightly brown, especially after repeated sterilization, but it has not been found to injure the fabric except in appearance. The muslin binder should be thick enough to avoid contamination of the contents of the pack during handling after sterilization. The gas cooking range described should be satisfactory for this purpose.

BIO LAB SYPHILIS TEST

To the Editor:—What can you tell me regarding the Bio Lab Syphilis Test, using one drop of blood? It seems as though several doctors over the country have bought the outfits and I am wondering if it is reliable and dependable. The makers are Bio Chemical Laboratories, Inc., Dayton, Ohio.

E. H. Brubaker, M.D., Flora, Ind.

ANSWER.—The Bio Lab Syphilis Test is published as a modification of the Ide test (Ide, Sobei, and Ide, *Tamoa: Ide Test—the New Color Test for Syphilis, J. Lab. & Clin. Med.* 21:1190 [Aug.] 1936) without stating what the modification is. The test is claimed to be "accurately diagnostic," but the literature on the Ide test is not unanimous on its value. The test is not supposed to require "specialized training," but tests for syphilis are based on complex interactions between colloids and they do require specialized training. The Ide or Bio Lab tests are not included among those which have been evaluated during the past five years by the American Evaluation Committee on tests for syphilis, which is functioning under the auspices of the U. S. Public Health Service, and no literature is available on the accuracy of the Bio Lab test.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, July 6, page 78.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, Sept. 11-13. Part III, June or July, to be given in medical centers having five or more candidates desiring to take the examination. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Written*. Various centers, Feb. 20. Final date for filing application is December 21. *Oral*. Cleveland, preceding A. M. A. convention. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: December 1940. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. October 21. Applications must be on file not later than September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 18-19. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral*. Cleveland, Oct. 5. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and written*. New Orleans, January 1941. Final date for filing application is December 15. Sec., Dr. Fremont A. Chandler, 61 "

AMERICAN BOARD OF PEDIATRICS: Memphis, Tenn., Nov. 17, preceding the annual meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral*. New York, December 18-19. Final date for filing application is October 8. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Boston, Sept. 26-29. Sec., Dr. Byrl R. Kirklm, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written*. Part I. Various centers, October 21. Final date for filing application is September 15. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Oral and written*. Chicago, February 1941. Applications must be on file not later than Oct. 15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

New York Endorsement Report

Mr. Herbert J. Hamilton, chief, Bureau of Professional Examinations, reports 105 physicians licensed by endorsement from January 15 through March 30. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
College of Medical "	"	N. B. M. Ex.
College of Physicians	"	California
Yale University Sch	"	N. B. M. Ex.
George Washington U	"	Maryland,
(1937) New Jersey		
Georgetown University School of Medicine.....	(1932)	Dist. Colum.,
(1933) Pennsylvania, (1936), (1938, 3)	N. B. M. Ex.,	
(1938) New Jersey		
Howard University College of Medicine.....	(1935)	Tennessee,
(1939) North Carolina		
Emory University School of Medicine.....	(1938)	N. B. M. Ex.
University of Georgia School of Medicine.....	(1934)	Georgia
Northwestern University Medical School.....	(1937)	California,
(1939) N. B. M. Ex.		
Rush Medical College	(1934)	Minnesota
University of Illinois College of Medicine.....	(1924)	Michigan,
(1938) Indiana		
State University of Iowa College of "	"	"
University of Louisville School of "	"	"
Johns Hopkins Univ. School of Me	"	"
University of Maryland School of Medicine and Col-	"	"
lege of Physicians and Surgeons.....	(1935)	New Jersey.
(1937), (1939, 2)	Maryland	
Boston University School of Medicine.....	(1938)	N. B. M. Ex.
Harvard Medical School	(1932)	Penna.,
(1933) N. B. M. Ex., (1936) North Carolina		
Tufts College Medical School.....	(1914)	Georgia, (1938) N. B. M. Ex.
University of Michigan Medical School.....	(1925), (1929, 2)	Michigan
Wayne University College of Medicine.....	(1939)	Tennessee
St. Louis Univ. School of Med. (1938) N.B.M.Ex., (1939, 4)		Tennessee
University of Nebraska College of Medicine.....	(1920)	Nebraska
Columbia Univ. College of Physicians and Surgeons (1937) N. B. M. Ex.		
Cornell University Medical College.....	(1938)	N. B. M. Ex.
Long Island College of Medicine.....	(1938, 4)	N. B. M. Ex.
New York Medical College and Flower Hospital (1936, 2), (1937, 4), (1938, 3)	N. B. M. Ex.	
New York Medical College, Flower and Fifth Avenue Hospitals	(1939)	Maryland
University of Buffalo School of Medicine.....	(1938)	N. B. M. Ex.
University of Rochester School of Medicine.....	(1934)	N. B. M. Ex.,
(1936) New Jersey		
Duke University School of Medicine.....	(1937)	N. B. M. Ex.
Eclectic Medical College, Cincinnati.....	(1938), (1939, 5)	Ohio
Ohio State University College of Medicine.....	(1937)	Ohio
University of Cincinnati College of Medicine.....	(1939)*	Ohio
University of Oklahoma School of Medicine.....	(1933)	Oklahoma

University of Oregon Medical School.....	(1937)	Maryland
Jefferson Medical College of Philadelphia... (1928), (1932)		Penna.,
(1932) Connecticut		
Medical College of the State of South Carolina.....	(1920)	Minnesota,
(1933, 2) South Carolina		
Baylor University College of Medicine.....	(1938)	Texas
University of Texas School of Medicine.....	(1936)	Texas
Marquette University School of Medicine.....	(1939)	N. B. M. Ex.
University of Manitoba Faculty of Medicine.....	(1929)	Saskatchewan
Laval University Faculty of Medicine.....	(1931)	Connecticut
McGill University Faculty of Medicine.....	(1934)	N. B. M. Ex.
Medizinische Fakultät der Universität Wien.....	(1935)	Maryland
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1920)	Germany, (1924) N. B. M. Ex.
Kaiser-Wilhelms-Universität Medizinische Fakultät, Strassburg	(1905)	Ohio
Ludwig-Maximilians-Universität Medizinische Fakultät, München	(1937)	New Jersey
Universität Heidelberg Medizinische Fakultät.....	(1914)	New Jersey,
(1930) Ohio		
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultása, Budapest	(1924)	New Jersey
Regia Università degli Studi di Firenze. Facoltà di Medicina e Chirurgia	(1928)	New Jersey
Regia Università degli Studi di Modena. Facoltà di Medicina e Chirurgia	(1927)	New Jersey
American University of Beirut School of Medicine.....	(1934)	N. B. M. Ex.
Licentiate of the Royal College of Physicians and of the Royal College of Surgeons of Edinburgh and of the Royal Faculty of Physicians and Surgeons of Glasgow	(1936)	Tennessee
Université de Lausanne Faculté de Médecine.....	(1935), (1937)	New Jersey, (1936) Ohio

* This applicant received the M.B. degree and will receive the M.D. degree on completion of internship.

Tennessee March Report

Dr. H. W. Qualls, secretary, Tennessee State Board of Medical Examiners, reports the written examination held at Memphis, March 20-21, 1940. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Twenty-five candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical "	"	"	85.3
New York University	"	"	88.2
University of Tennes	"	"	83.6,
84.1, 84.3, 85.3, 85.4, 86.1, 86.2, 87, 87, 87, 88, 88.1, 88.2, 88.3, 89.3, 89.5, 89.5, 90.1, 90.9, 90.9, 91.3, 91.8			

Six physicians were licensed by endorsement from February 2 through April 27. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois.....	(1898)	Illinois
University of Louisville School of Medicine.....	(1935)	Kentucky
Johns Hopkins University School of Medicine.....	(1936)	Maryland
University of Michigan Medical School.....	"	Maryland
Ohio State University College of "	"	Ohio
University of Tennessee College of "	"	M. Ex.

Oregon January Report

Miss May Casey, assistant secretary, Oregon State Board of Medical Examiners, reports the written examination held at Portland, Jan. 9-11, 1940. The examination covered eleven subjects and included seventy-two questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Oregon Medical School.....	(1935)		89
University of Wisconsin Medical School.....	(1937)		86

Eight physicians were licensed by reciprocity and three physicians were licensed by endorsement from January 10 through April 10. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical "	"	"	California
State University of "	"	"	Iowa
University of Minne	"	"	Minnesota
University of Nebraska College of Medicine.....	(1935)		Nebraska
University of Oregon Medical School.....	(1933), (1934)		Washington
University of Manitoba Faculty of Medicine.....	(1925)		Arizona
University of Toronto Faculty of Medicine.....	(1934)		Minnesota

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
Washington University School of Medicine.....	(1934), (1935)	N. B. M. Ex.
Duke University School of Medicine.....	(1938)	N. B. M. Ex.

Book Notices

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1939 with the Comments That Have Appeared in The Journal. Cloth. Price, \$1. Pp. 205, with 5 illustrations. Chicago: American Medical Association, 1940.

Only seven of the thirty-five reports listed in this annual collected report are of the familiar "Not Acceptable" or condemnatory type. Two reports announce omission of products from N. N. R., one being off the market. The remainder, far superior in bulk as well as in number, are concerned with educational and constructive considerations. This trend has been noticeable in recent years; it reflects the great predominance of the constructive over what may be called the destructive side of the Council's work of promoting rational therapeutics.

The educational reports touch three fields on which lie the front lines of present day therapeutics progress—chemotherapeutics, endocrines and vitamins. Two reports on sulfapyridine deal with the status and Council acceptance of commercial brands. The report on Neoprontosil recognizes that term as the Winthrop Chemical Company's proprietary name for 4-sulfonamide benzene-2-azo-1-hydroxy-7-acetylamino naphthalene-3:6-disodium sulfonate, and azosulfamide as the nonproprietary name for the same substance. The articles on Dilantin Sodium, Sobisminol Mass and Sobisminol Solution are status reports which accompanied the descriptions of accepted brands, a type of article increasingly used by the Council. Dilantin sodium is the new drug used in the treatment of epilepsy and has been accepted by the Council with carefully stated limitations for its use; sobisminol mass and sobisminol solution are new soluble bismuth preparations for use in the treatment of syphilis; they are noteworthy in that sobisminol mass has been shown to be effective when used orally. The reports on racéphedrine and nikethamide deal with nomenclature; these terms are recognized as nonproprietary names for racemic ephedrine (the sulfate and hydrochloride are also recognized) and pyridine- β -carboxylic acid diethylamide respectively; the latter was introduced into medicine under the proprietary name Coramine-Ciba and was the subject of a preliminary report by the Council in 1929 (THE JOURNAL, June 1, 1929, p. 1837).

The status report on questions concerning vitamins compiled by the Cooperative Committee on Vitamins of the Councils on Pharmacy and Chemistry and on Foods is becoming an almost annual event, awaited for the revisions of the "Allowable Claims" found acceptable for the various vitamins. This year's revisions are not extensive but the report is noteworthy for the reemphasis of the Council's stand on the subject of vitamins and vitamin mixtures. Alas, the Council's is but one clear, authoritative voice of rationality in today's whirlwind of polyvitamin and polyvitamin-mineral absurdities foisted on the gullible public by astute and sophisticated advertising technic. The preliminary and supplementary reports by Snell and by Snell and Butt on the new principle for active hemorrhagic diathesis known as "vitamin K" are timely and noteworthy.

The leadership of the Council in matters of endocrine therapeutics and nomenclature is well sustained by such reports as Chorionic Gonadotropin, Assay Standards for Chorionic Gonadotropin, Stilbestrol and the Present Status of Testosterone Propionate: Three Brands, Perandren, Oreton and Neo-Hombreol Not Acceptable for N. N. R. No brand of any of these has been accepted and these reports are excellent justification of the Council's intelligent and well informed conservatism in this as in other matters.

Three "special" reports are worthy of mention. One is the warning report on the danger of intra-urethral injection of solutions of local anesthetics, a reaffirmative strengthening of previous Council pronouncements. One is the Council statement Manganese in the Treatment of Dermatologic Disorders, which is buttressed by the conclusive and well documented paper of Dr. Maurice Sullivan, considered and sponsored by the Council. The third is the Study of the Promiseous Use of the Barbiturates, Their Use in Suicides, a paper by Dr. W. E. Hambourger based on a review of medical literature and study of vital statistics. This study was authorized by

the Board of Trustees of the A. M. A. and will be followed by other papers dealing with other aspects of the problem.

The present annual volume of Council reports is somewhat larger than usual and somewhat above the average issue in interest.

Good Health and Bad Medicine: A Family Medical Guide. By Harold Aaron, M.J., Medical Consultant to Consumers Union of United States, Inc. Cloth. Price, \$3. Pp. 328. New York: Robert M. McBride & Company, 1940.

This book, designed as a family medical guide, contains much interesting information. It is composed for the most part of what should be, by this time, well known suggestions for the maintenance of health. In some respects it goes further than the ordinary health guide, especially as it attempts to inform the reader of objectionable items which he might otherwise purchase for self medication for treatment of his own condition. Other items are recommended with carefully guarded statements as to the limitations of their use. In some cases the references for this evaluation of products include the various Councils, Bureaus and laboratories of the American Medical Association, but, needless to say, for the most part they are based on the reports of Consumers Union itself.

The book opens with a section on first aid and a description of a family medicine cabinet. This is followed by clearcut discussions of the various symptoms and disorders which are all too frequently cared for by self medication. The author is careful to warn repeatedly that certain conditions require the immediate attention of a physician and that others require his services if they are not amenable to the simplest remedies. In connection with dentifrices, the reader is referred to the American Dental Association, and for hearing aids, air filters and acceptable sun lamps for home use to the American Medical Association's Council on Physical Therapy. The vitamin preparations included are those which appeared in New and Nonofficial Remedies for 1939, and the author concurs in the Council on Pharmacy and Chemistry's decisions with regard to the "shot-gun" vitamin preparations. Warnings against the use of stimulants and drugs such as acetanilid and the bromides are well detailed. On the subject of diabetes the author lists all the remedies which have been declared to be fake or totally worthless by either the Council on Pharmacy and Chemistry or the Bureau of Investigation of the American Medical Association. The author concludes by stating that, if consumers learn from this book that medical advice appearing in advertisements should be taken with the proverbial grain of salt, the author will consider his work a success. It is doubtful whether he realizes that he has failed to include definite statements suggesting where additional information may be obtained concerning "patent medicines" and the advertising claims made for them.

There are some statements in the book which are open to question. For example, "The new Food and Drug law does not require that the presence of quinine be stated on the label" and "The only drug remedy that has been found to be of real value in the treatment of a cold is a combination of codeine and papaverine, or codeine alone." With some exceptions, however, the author's statements are in accordance with scientific fact.

La selva peruana: Sus pobladores y su colonización en seguridad sanitaria. Por el Dr. Carlos Enrique Paz Soldán, director, y Dr. Maxime Kuczynski-Godard, jefe de laboratorios del Instituto de medicina social de la Universidad de San Marcos, Lima. Paper. Pp. 68, with 100 illustrations. Lima: Ediciones de "La Reforma Médica," 1939.

This is a general discussion of the Indians of the Peruvian selva and of the possibilities for colonizing the selva. The latter is made up of the mysterious tropical lands near the Amazon River, which are rich in natural resources and apparently not good for the health of Peruvians other than the autochthonous Indians. The first chapter is by Professor Kuczynski-Godard, head technician of the Laboratories of the Instituto de Medicina Social of the University of San Marcos of Lima and also head of a scientific expedition to the selva which was organized by the institute as a preliminary survey in relation to colonization of the selva. The chapter is an ecologic study and a report of observations carried on during a long stay of the expedition in the selva, on the actual living

conditions of the people in relation to the cosmologic, geologic and social environment and also in relation to regional pathology. The second chapter is written by Dr. Carlos Enrique Paz Soldán, head of the Instituto de Medicina Social of the University of Lima and also organizer of the scientific expedition to the selva. The illustrations were taken during the expedition to the colony of the Perené River. They show beautiful scenes of the selva mountains and river, different racial types of Indians, housing of colonists and Indians and Indians suffering from regional diseases, most frequently malaria and ancylostomiasis. The whole collection of illustrations appears to be an ethnographic atlas of the Peruvian oriental selva.

Applied Anatomy: Functional and Topographical. By Robert H. Miller, M.D., Associate Professor of Anatomy in the University of Tennessee College of Medicine, Memphis. Cloth. Price, \$6.50. Pp. 484, with 71 illustrations, including 16 colored plates. Philadelphia: Lea & Febiger, 1938.

Dr. Miller was a surgeon. He is now a professor of anatomy; this book indicates that he has long been a biologist. Evolution, both anatomic and physiologic, comes in for nearly as much consideration as does clinical anatomy. The book deals with those facts of anatomy which are of most biologic significance or of most direct clinical application. It is briefer than are most textbooks on the subject because it makes no attempt to be encyclopedic, but it is well arranged and covers the important parts of the field. The views expressed are logical and documented by constant references to recent literature. Medical students will find it interesting, instructive and a valuable introduction of clinical work. It will be of great service to them in directing their attention to those relatively few among the innumerable anatomic facts which are most valuable, significant and applicable. Physicians will be interested in the presentation of the biologic as contrasted with the clinical view of many of the discussions.

The Surgery of Pain. By René Leriche, M.D., LL.D., F.R.C.S., Professor of Clinical Surgery, University of Strasbourg, Strasbourg. Translated and edited by Arelkald Young, B.Sc., M.B., C.M., Regius Professor of Surgery, University of Glasgow, Glasgow. Cloth. Price, \$6.50. Pp. 512, with 18 illustrations. Baltimore: William Wood & Company, 1939.

The author is a person whose name has been associated for many years with the subject and who has written many articles on the theoretical, practice and experimental aspects of this problem. He is a worldwide authority on the subject at hand. From the nature of the book, which is really a series of lectures based on a theory of pain with an attempt at scientific investigation and compilation of facts, it is apparent that one must read the book in order to follow logically the author's concepts. The reader will be conscious of the enthusiasm of the author and will be easily and quickly won over. The practical application of the theory is not quite as convincing because of the elusive nature of pain. Leriche attacks the problem of pain not merely as a symptom but as a disease entity. The first two chapters cover the problem of pain in the light of surgical investigation and the physiologic condition of the pain—malady—general considerations regarding the surgery of pain. His work included ramisections which in the past decade have been supplanted by ganglionectomies because of surgical convenience and also splanchnic resections. He discusses surgery of the sympathetics and of the endoerines, especially adrenals and parathyroids. His diagnostic and therapeutic methods of local infiltrations with procaine hydrochloride and of direct infiltrations of the sympathetic trunks has been remarkably useful. The chapters on clinical entities include trifacial neuralgia, post-traumatic progressive spreading neuralgias, nerve injuries, causalgia and painful amputation stumps. Several chapters are devoted to vasoconstriction and such entities as Raynaud's disease and scleroderma. The subjects of arteritis and angina pectoris are well worth reading because of the insight into the cause of pain and the methods of obtaining relief. There are a chapter on cutaneous cicatrices and several chapters on visceral pain. The book closes with the pain of inoperable tumors and its treatment and a chapter entitled "What is Physical Pain?" In the translator's preface there is much praise for the author's work and great respect for his theories and practice in the alleviation of pain through the attack on the sympathetics and in the diagnostic value of the abolition of pain by regional infiltration with pro-

caine. The book can be recommended highly for its attempt to solve the problem of pain, and the author will undoubtedly contribute more and more toward the alleviation of pain with the progress of time.

Fractures. By Paul B. Magnuson, M.D., F.A.C.S., Associate Professor of Surgery, Northwestern University Medical School, Chicago. Third edition. Cloth. Price, \$5. Pp. 311, with 317 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1939.

The author adheres to his original purpose in writing this book, which was to present the subject from a broad point of view. He calls attention to the fact that the approach to the problems in the treatment of fractures has gone through a state of evolution, and he incorporates these trends in the present edition. The author presents those methods which he has found from experience to be worthy of trial. He has made a considerable addition to the discussion of first aid in the treatment of compound fractures, emphasizing the necessity for standardization of metal plates. The section on pathologic changes occurring in fracture lesions has been revised in accordance with the views of the American College of Surgeons. The operative treatment of fractures of the head of the humerus and the treatment of both bone fractures of the forearm by use of Kirchner's method are discussed. The section on fractures of the neck of the femur, a subject on which the author has written much good material, is also amplified. The whole work has been rewritten and reillustrated. The numerous beautiful line drawings by Shepard are especially clear and instructive.

Histological Technique for Intracranial Tumours. By Dorothy S. Russell, M.D., Member of Scientific Staff, Medical Research Council, Attached to Bernhard Baron Institute of Pathology, the London Hospital. Cloth. Price, \$2.50. Pp. 71, with illustrations. New York & London: Oxford University Press, 1939.

This purely technical book should be of great value to all histologic technicians. It contains most of the recognized techniques for the gross and microscopic preparation of all types of neurologic specimens with such personal modifications as Dr. Russell has deemed valuable in her extensive experience. She is to be especially commended for her appreciation of the limitations of classifications of such specimens by pure histologic staining methods. She is also wise in adding methods of rapid sectioning of tissues for immediate study during operations. Fortunately she considers the immediate practical value of her technical procedures rather than pure academic research, although many of the techniques might well be used for that purpose. The book contains six photographic plates which serve as excellent examples of beautiful histologic and photographic technique.

Orthodigila: Procedure and Technique. An Introductory Text for Students and Practitioners of Podiatry. By Harry S. Elsenberg, Pod.G. Paper. Price, \$1.50. Pp. 166, with 153 illustrations. Brooklyn, N. Y.: The Author, 1939.

The author defines the title of his book as a study of the development of the toes. He seeks to determine factors which determine the growth of toes to the end that normal, functional and anatomic relationship between the toes and the foot may be realized. He considers the subject a biologic problem with mechanical aspects. The aims and benefits of orthodigila are said to be the correction, restoration of function, treatment and prevention of foot deformities, relief from pain, and the elimination of deformities. Most of the diagrams are crude and many fail to instruct. The book is of no value whatever to the practicing physician.

Foot Orthopaedics. By Otto N. Schuster, Litt.B., Pod.G., Adjunct Professor Podiatric Orthopaedics, The First Institute of Podiatry, New York. Edited by Maurice J. Levi, M.D., and Herman Schelmsberg, M.D. Second edition. Cloth. Price, \$7. Pp. 523, with illustrations. Albany, N. Y.: J. B. Lyon Company, 1939.

The author has made numerous additions to the first edition of his book. Several chapters have been rewritten, new illustrations added and some old ones deleted. One of the added chapters deals with the application of plaster of paris in relation to foot appliances. Many roentgenograms have been included in this edition. Many of the subjects are discussed briefly, which is necessary in order to keep the book within the confines of a handy volume. It is not clear why surgical procedures such as the Whitman astragalectomy are given in a book for chiropodists.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Liability of Employer for Medical and Hospital Treatment in Excess of Statutory Period.—In the course of her employment, Feb. 21, 1936, the plaintiff was struck on the head by a broken belt. The industrial commission of North Carolina approved an agreement for compensation entered into between her and her employer. While she was under treatment for her industrial injury a "serious mental disorder" developed and she was institutionalized in two different private sanatoriums. In February 1938, the employer petitioned the industrial commission for a release from liability for the expense of further medical and hospital treatment, contending that he had furnished treatment for the time required by the Workmen's Compensation Act of North Carolina and that unless further treatment would "tend to lessen the period of disability" he was not liable for further expenses. After a hearing, during which the testimony of three physicians was heard, the industrial commission denied the petition and found that the plaintiff was suffering from an incurable mental condition, dementia praecox, and that it was necessary to provide her "some kind of care at all times." The commission ordered the plaintiff transferred to the State Hospital at Morgantown, N. C., which transfer was made July 1, 1938, and further ordered the employer and his insurer, the defendants, to pay the cost of such hospitalization. The defendants then appealed to the superior court, Gaston County, which remanded the cause to the commission for a finding as to whether or not additional hospitalization and treatment would tend to lessen the period of disability. The commission without hearing further evidence made a specific finding that "additional hospitalization and treatment would tend to lessen the period of disability," and the defendants appealed again to the superior court, Gaston County. From a judgment of that court sustaining the commission's finding, the defendants appealed to the Supreme Court of North Carolina.

The questions to be determined, said the Supreme Court, are: 1. Is there sufficient competent evidence to support the commission's finding that additional hospitalization and treatment would tend to lessen the period of plaintiff's disability? 2. If not, when the industrial commission finds that a claimant is permanently and totally disabled as a result of an accidental injury arising out of and in the course of employment may the commission in its discretion award medical, surgical, hospital and other treatment for an indefinite period of time? Section 25 of the workmen's compensation act of North Carolina requires an employer to provide a workman injured in the course of his employment with necessary medical and hospital care "for a period not exceeding ten weeks from date of injury to effect a cure or give relief, and for such additional time as in the judgment of the commission will tend to lessen the period of disability." It is plain from this language that medical, surgical, hospital and other treatment must be provided by the employer for a period of ten weeks if such treatment is necessary to effect a cure or to give relief. Treatment may not be required for an additional time unless it "will tend to lessen the period of disability." Whether such additional treatment will tend to lessen the period of disability is a question of fact to be ascertained by the industrial commission on competent evidence. The court, however, did not believe that the commission was warranted in the instant case in making the finding that it did as to the effect of additional hospital treatment to be rendered to the plaintiff. All the physicians who testified before the commission agreed that the plaintiff's condition is incurable, that her psychosis is beyond human control and can be influenced only in minor features by treatment of any kind and that nothing remains to be done but to provide custodial care. There was no evidence whatever before the commission that further treatment would tend to lessen the period of the plaintiff's disability. On the contrary, the commission stated in the course of its first finding that the plaintiff had "sustained an injury by accident

arising out of and in the course of her employment, resulting in permanent total disability." That finding terminated the liability of the employer for further treatment.

Another provision of section 25 of the workmen's compensation act provides that "in case of a controversy arising between the employer and employee relative to continuance of medical, surgical, hospital, or other treatment, the Industrial Commission may order such further treatment as may in the discretion of the commission be necessary." In the judgment of the court this provision must be read in connection with the rest of that section. When so considered, the exercise of discretion by the commission as to the necessity for treatment beyond the ten weeks' period can come into play only on a proper finding by it that additional treatment "will tend to lessen the period of disability." As already stated, such a finding in the instant case was not supported by the evidence.

The court accordingly, in effect, relieved the employer and his insurer from liability for further treatment and custodial care.—*Millwood v. Firestone Cotton Mills (N. C.)*, 2 S. E. (2d) 568.

Workmen's Compensation Acts: Death from Unintentional Poisoning While Under Treatment for Industrial Injury.—A workman in the course of his employment sustained an industrial injury which necessitated the amputation of a portion of a toe six months later, May 26, 1936. His attending physician directed him to bathe the affected foot in a solution of mercury bichloride at stated times and gave him tablets of mercury bichloride with which to prepare the solution. Later the physician prescribed "sedative tablets" to be taken if the patient became uncomfortable from pain. The physician discharged the patient, June 16, "although the wound was still healing." On June 20, while intending to take a "sedative tablet" to relieve his pain, the workman by mistake swallowed a mercury bichloride tablet and died as a result thereof. His widow's claim for compensation under the New York workmen's compensation act for his death was denied by the State Industrial Board and she appealed to the supreme court, appellate division, third department, New York.

From the evidence adduced, said the court, it was apparent not only that the pain which the workman suffered following the amputation but also the taking of the sedative were the result of the employment. The painful injury and the attempt to minister thereto flowed directly from the employment. The catenation from the original industrial accident to the death about six months later was continuous. Had the physician by mistake administered the mercury bichloride tablet in place of a sedative the right to an award would not be open to question. *Parchesky v. Kroll Bros., Inc.*, 267 N. Y. 410, 196 N. E. 308. The court could see no distinction in the fact that the workman made the same mistake while attempting to relieve his pain in the manner and with a medicine prescribed by the physician. The court held that the death under the circumstances was compensable as an accidental injury arising from employment, and so it remanded the case to the industrial board for further proceedings in harmony with its decision. Subsequently the industrial board awarded compensation to the widow, which award was affirmed by the supreme court.—*Broten v. New York State Training School for Girls (N. Y.)*, 11 N. Y. S. (2d) 849; 19 N. Y. S. (2d) 901.

Society Proceedings

COMING MEETINGS

American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.
National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
Virginia Medical Society of White Sulphur Springs, W. Va., July 29-31. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.
Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
West Virginia State Medical Association, White Sulphur Springs, July 29-31. Mr. Joe W. Savage, Public Library Bldg., Charleston, Executive Secretary.
Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

59:931-1166 (May) 1940

Congenital Cranial Osteoporosis: Its Etiology and Significance: Study of 800 Newborn Infants. O. Reiss and Elena Boder, Los Angeles.—p. 931.

Study of 240 Breast-Fed and Artificially Fed Infants in the St. Louis Area: II. Incidence of Rasbes and Gastrointestinal Disturbances in Breast-Fed Infants and in Infants Fed on Fresh Milk Formulas and on Acidified (Lactic Acid) and Nonacidified Evaporated Milk Formulas. Edith C. Robinson, St. Louis.—p. 1002.

Factors Influencing Appearance of Centers of Ossification During Early Childhood: II. Comparative Study of Degree of Epiphyseal Ossification in Infancy Under Varying Conditions of Diet and Health. C. C. Francis, Cleveland.—p. 1006.

*Enuresis: Study of Causes, Types and Therapeutic Results. L. Stockwell and C. K. Smith, Kansas City, Mo.—p. 1013.

*Tuberculosis: Follow-Up Study of Children at Lymanhurst Health Center. C. A. Stewart, Minneapolis.—p. 1034.

Interchangeability of Zinc Crystalline Insulin and Amorphous Insulin. R. L. Jackson, J. D. Boyd and Thelma Smith, Iowa City.—p. 1050.

Probable Mechanism of "Physiologic" Hypoproteinemia of the Newborn. L. M. Tocantins, Philadelphia.—p. 1054.

Gonorrheal Vaginitis in Children: Review of Literature. R. A. Benson and I. Weinstock, New York.—p. 1083.

Enuresis.—From an analysis of 100 representative children observed in the enuresis clinic Stockwell and Smith discuss the psychosomatic significance, the types of enuresis, the known facts about bladder function, the causative factors and the results of treatment. Enuresis in their experience is of three types: organic, 13 per cent; neuromyogenic, 37 per cent, and psychogenic, 50 per cent. Diagnosis of the type of enuresis before treatment is instituted is extremely important. A simple cystometric examination was a distinct aid in the analysis of function. The average age of the patients (sixty-three boys and thirty-seven girls) was 9 years. In fifty-nine who later had enuresis normal control had once developed—at the age of 16½ months in boys and 17½ in girls. Forty-one had nocturnal enuresis only, forty-seven nocturnal enuresis plus diurnal frequency but not incontinence; ten diurnal as well as nocturnal enuresis and two diurnal but not nocturnal enuresis. The therapeutic methods in addition to correction of physical defects and simple training are: (1) for the spastic bladder, atropine therapy plus aqueous distention, (2) for the atonic bladder, stimulation of the neck of the bladder and in severe cases mecholyl (acetyl-beta-methylcholine) and acetylcholine, (3) for the strongly expulsive bladder of small capacity, simple regular aqueous distention and (4) for nocturnal enuresis plus poor sphincter action, physiologic dosage of morphine at bedtime. Treatment was directed toward establishing a conditioned reflex by developing in the child a strong conscious effort to control the distended bladder, an effort which establishes neural pathways and cerebral interpretation of vesical function. This treatment worked best on essentially normal bladders. Patients with definite psychogenic enuresis responded well to simple psychotherapy, encouragement, education and adjustment of personal and social problems. Results indicated that 64 per cent of the patients were cured and 21 per cent improved (14 per cent of these had recurrences occasionally); 15 per cent were classed as unsatisfactory for various reasons.

Tuberculosis in Children.—Stewart analyzed the records of 10,003 children who entered the Lymanhurst Health Center between May 1921 and July 1932. The ages ranged from 3 months to 20 years and averaged 9 years. Initial reactions

to tuberculin were negative for 7,107 and positive for 2,896. Initial roentgenograms of the chest were made of 84.3 per cent of the uninfected and of 95.5 per cent of the infected children. The lungs of 92.9 per cent of those with negative reactions and 57 per cent of the tuberculin-sensitive group were interpreted as normal. The incidence of roentgenographically demonstrable lesions considered nontuberculous tended in general to increase gradually in successive age groups. Relatively benign pneumonic infiltrations of pulmonary tuberculosis were found in 166 members of the infected group. The incidence of such lesions reached a maximum at about the third year of life and then diminished. The general tendency of these lesions was first to persist and later to resolve slowly. Calcified and fibrosed deposits were revealed by 2.8 per cent of the initial roentgenograms of the children with negative reactions, increasing slightly with advancing age. Calcified and fibrosed deposits were disclosed by 30.6 per cent of the initial roentgenograms of the infected children, increasing rapidly until the age of 8.5 years, after which it showed no consistent change. The initial roentgen study of 2,767 of the tuberculous children disclosed forty-nine with chronic pulmonary tuberculosis of the adult type. This form of the disease made its first appearance at the seventh year of life and tended to increase in relative frequency in each successive age group. Follow-up data derived from repeated roentgen studies, tuberculin tests or verbal inquiry were obtained for 80.9 per cent of the children with negative reactions and for 85.2 per cent of the infected group. The uninfected group were traced for an average of 6.1 years and the infected group for 6.9 years. Chronic pulmonary tuberculosis was acquired by sixteen of the 5,747 traced children whose initial tuberculin reactions were negative. Of the 2,467 traced children with initial positive reactions, 2,418 presented no evidence of chronic pulmonary tuberculosis at the time of the first examination. During the course of the follow-up study such disease was acquired by fifty-eight. During the follow-up the incidence of roentgenographically normal lungs decreased from 53.9 to 36.9 per cent in the infected group and the incidence of primary pneumonic tuberculous infiltrations decreased from 7.9 to 0.7 per cent. This change resulted from spontaneous resolution. The incidence of calcified and fibrosed deposits changed from an initial 31.6 per cent to a final 53.1 per cent. This change resulted from the appearance of these lesions in many of the infected children whose initial roentgenograms revealed no pathologic conditions. The incidence of chronic pulmonary tuberculosis increased from 2.7 to 6 per cent. During the course of the follow-up study chronic pulmonary and military disease, tuberculous meningitis and osteo-articular tuberculosis were acquired by nineteen members of the originally uninfected group and by ninety-eight members of the infected group.

American Journal of Hygiene, Baltimore

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Blood Chemistry Findings in Early Trichinosis of Dogs. E. Hartman, M. Foote and H. B. Pierce, Burlington, Vt.—p. 74.

American Journal of Ophthalmology, St. Louis

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- Blindness in Cattle Due to Papilledema: Autopsy Report on Six Cases. J. O. Wetzel, Lansing, Mich., and L. A. Moore, East Lansing, Mich.—p. 499.
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- Keratomalacia and Cystic Fibrosis of Pancreas. R. C. Gamble, Chicago.—p. 539.
- Alterations in Angioscleromas Following Oral Administration of Benzedrine Sulfate. C. M. Rosenthal, Brooklyn, and C. P. Seitz, University, Ala.—p. 545.
- New Apparatus for Extraction of Cataract by Suction. H. Ferrer, Havana, Cuba.—p. 550.
- Transmission of Swimming-Bath Conjunctivitis to Monkeys. L. A. Julianelle, St. Louis.—p. 554.

Annals of Surgery, Philadelphia

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- Role of Irradiation in Treatment of Carcinoma of Breast. H. H. Trout, Roanoke, Va.—p. 700.
- *Scalenus Anticus Syndrome With and Without Cervical Rib. J. M. Donald and B. F. Morton, Birmingham, Ala.—p. 709.
- *Cervicobrachial Syndrome: Discussion of Etiology with Report of Twenty Cases. K. H. Aynesworth, Waco, Texas.—p. 724.
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- *Penetrating Wounds of Abdomen: Analysis of Forty-Six Personal Cases. A. H. Storek, New Orleans.—p. 775.
- Factors of Mortality in 4,000 Operations on External Biliary System. C. G. Heyd, New York.—p. 820.
- Immediate and End Results of Cholecystectomy. W. H. Parsons, Vicksburg, Miss.—p. 831.
- *Surgical Management of Stone in Common Bile Duct: Follow-Up Studies, with Special Reference to Graded Dilatation of Sphincter of Oddi. A. W. Allen and R. H. Wallace, Boston.—p. 838.
- *Diagnosis and Treatment of Acute Pancreatitis. J. J. Morton and S. Widger, Rochester, N. Y.—p. 851.
- Maintenance of Pregnancy in Human After Removal of Both Ovaries: Case Report. W. B. Russ, San Antonio, Texas.—p. 871.
- Modified Kondoleon Operation for Sclerosed Leg with Ulceration. F. W. Bancroft, Margaret Stanley-Brown and R. F. Taylor, New York.—p. 874.

Scalenus Anticus Syndrome With and Without Cervical Rib.—Donald and Morton studied twenty-one cases of the cervical rib and scalenus anticus syndrome. Of the sixteen patients that have already received operative treatment, thirteen were without cervical ribs, two showed supernumerary ribs and one presented an abnormal first rib. This indicates that the scalenus anticus syndrome occurs much more frequently than do cervical ribs. Two of the remaining five cases, in which operation has been temporarily postponed, showed x-ray evidence of a cervical rib. The ages of the twenty-one patients ranged from 15 to 54 years, with an average of 37 years. The majority occurred in the fourth (nine) and fifth (five) decades. Direct trauma preceding the onset of symptoms could be demonstrated in only one of the twenty-one cases. In two others the trauma was attributed to faulty position while under anesthesia, followed immediately by the development of symptoms typical of the syndrome. Excessive occupational strain was a significant factor in eight cases. The preponderance of cases in the fourth and fifth decades may possibly be attributed to regressive muscular changes that occur at this time and result in drooping of the shoulders. The characteristic increase of pain at night may be accounted for by pressure from behind as the shoulders are brought forward against the scalenus anticus muscle while in the prone position. The symptoms of cervical rib and scalenus anticus syndrome are similar and in view of the fact that the scalenus anticus muscle is the primary factor in the production of neurocirculatory compression, whether a cervical or an abnormal first rib is present, it would seem appropriate to group the two conditions under the term "scalenus anticus syndrome," designating whether a cervical rib or an abnormal first rib is present. The surgical indications

(scalenotomy) are the same and results are usually excellent. Fourteen patients have had complete relief from symptoms. Scalenotomy is not indicated in all cases, as many are mild and will respond to conservative therapy. The symptoms in the milder cases are not progressive but subject to remissions and exacerbations. Because of the frequent gradual onset and bizarre picture a positive diagnosis is often difficult. A neurologic examination is indicated in all cases. Conditions causing difficulty in the differential diagnosis are infectious neuritis, arthritis of the shoulder joint, cervical arthritis, subacromial bursitis and neurosis.

Cervicobrachial Syndrome.—Aynesworth believes that the Naffziger classification, neuritis of the brachial trunks, of the scalenus syndrome is too limited and that the vascular and nerve trunk symptoms should be expressed by a more inclusive term. The term "cervicobrachial syndrome" does not define the disease but it does give a comprehensive and an anatomic concept which is accurate and inclusive. The author has observed twenty cases in which the diagnosis was confirmed by operation or subsequent history. Sixteen of these patients have come under observation since the role of the scalenus anterior muscle has been understood. Of ten patients operated on, all but one were relieved of symptoms. The exception had only partial relief. X-ray examinations on patients not operated on confirmed the presence of cervical ribs when present and the neurologic and vascular examinations elicited the same observations as on patients operated on. All gave a history of traumatism. The symptoms under the heading cervicobrachial syndrome may be classified into neurologic symptoms, vascular symptoms or a combination of the two. These classifications arise from and are an expression of the major pathologic changes of the disease. The causes are similar but the pathologic processes are different. Compression of nerve tissues produces numbness, pain, paralysis and loss of function; compression of vascular structures results in moderate pain, edema, swelling, obstruction of the blood flow ending in clotting in the vessels and, if serious enough, death of the tissues supplied by these vessels. The location of the pathologic changes is confined to a small area, but one which is full of nerves and blood vessels, surrounded by muscles and osseous structures which have undergone great and vital changes in the course of evolution and embryology. Many of the diseases in this small region are the result of developmental defects. The theories of the etiology of the cervicobrachial syndrome are: (1) compression of the nerve trunks, (2) injury to the nerve trunks, (3) injuries to the sympathetic and the vasomotor nerves, (4) traumatism of the scalenus anterior muscle, (5) embryologic defects, (6) postural or functional defect, (7) narrowing of the upper thoracic cage as a result of adjacent infections or anatomic defects, (8) acute infections producing myositis and (9) intermittent traumatism to the subclavian artery.

Penetrating Wounds of Abdomen.—Storek reports forty-six cases of penetrating wounds of the abdomen, thirty-five of which were gunshot and eleven stab wounds. The symptoms associated with penetrating wounds of the abdomen are frequently indefinite. Pain is often slight or absent. Wounds which occur by way of the gluteal, sacral or perineal regions are particularly likely to be overlooked because early symptoms are frequently absent. The recognition of associated injuries, particularly those of the chest, is important in the management. Exploratory celiotomy should be performed when uncertainty concerning penetration of the abdomen exists. A short interval between the time of injury and the operation usually favorably influences the outcome and operations should be delayed until patients have at least considerably recovered from shock. Prolonged shock and hemorrhage produce irreversible deleterious effects and should be combated early. In the presence of considerable hemorrhage, transfusions during and shortly after operation totaling as much as 3,000 cc. of blood may be necessary. Transfusions should, whenever possible, displace the administration of saline, dextrose infusions or stimulant drugs. The ricochet of bullets and the position of the patient at the time of injury as compared with his position on the operating table accounts for apparently bizarre courses of bullets. Unexpected and unpredictable visceral injuries due to the position of the patient or the phase of respiration at the time of injury were observed frequently. Perforations of hollow

or solid viscera were only slightly less frequent among the patients who lived than among those who died. Extraperitoneal hemorrhage or hemorrhage between the leaves of the mesentery is likely to obscure important injuries. Drains introduced into the peritoneal cavity are undesirable, but drainage of the abdominal wall should be instituted when hollow viscera have been perforated. Silk or cotton sutures and ligatures are superior to catgut for the repair of hollow viscera and for the closure of the abdominal wall. Irrigation or lavage of the peritoneal cavity is usually futile, but it is desirable to suck out or pick out from the peritoneal cavity liquid blood, blood clots, detached particles of viscera, intestinal contents and foreign bodies. The avoidance of enemas and flushes aids in preventing or reducing the severity of ileus and peritonitis. Biologic preparations and chemotherapeutic agents may prove of value in reducing the mortality from peritonitis resulting from penetrating abdominal wounds. Lyophilized serum or whole blood transfusions are sometimes necessary to maintain plasma protein at a normal level postoperatively. Atelectasis and pneumonia are frequent complications. The mortality of the eleven cases of stab wounds was 27.2 per cent and of the thirty-five cases of gunshot wounds 40 per cent. Recent advances in the treatment of shock, hemorrhage, ileus and peritonitis should help in lowering this high mortality.

Surgical Management of Bile Duct Stones.—According to Allen and Wallace, from October 1930 to October 1935 1,228 patients were operated on in the Baker Memorial and the Massachusetts General hospitals for disease of the extrahepatic biliary system. Of these, 395 had exploration of the common bile duct, 231 had instrumentation of the papilla (with an average dilation of 7 mm.) and 164 had nothing more done than the removal of the calculi and the determination that the papilla was patent. From October 1935 to October 1939, 860 additional patients were subjected to operations. Of these, 380 had common duct exploration and 330 had their papillae dilated; only fifty had a simple exploration. It is, therefore, apparent that more of the staff have become convinced of the safety and rationale of routine, gentle and gradual dilation of the duct outlet. Such dilation does not increase the mortality. In fact, it would seem that the procedure is attended by less risk than exploration alone. It would seem that at least one of Bakes's claims may have been justified, i. e. dilation enhances the flow of bile into the duodenum. There were more postoperative pulmonary complications in the group that had had dilation of the papilla. Fatal bile peritonitis occurred in four of the patients who had dilation, while none occurred in the non-dilated group. However, the authors believe that the technical difficulties of drainage accounting for these deaths have been corrected. There was a lower though not marked or significant percentage of mortality among patients who had dilation of the papilla. The nonfatal complications were greater in patients who did not have instrumentation of the papilla. They were evident in prolonged external bile drainage, increased hospital stay and secondary operations. Serious ascending infection did not follow instrumentation of the papilla. Duodenal reflux occurred in only one case, and this cleared up spontaneously. Late cicatricial constriction of the dilated papilla did not occur. The permanence of the dilation in the average case is doubted. In large ducts dilated to 1 cm. the sphincteric action may be lost. Under these circumstances, the health of the patient was not interfered with.

Acute Pancreatitis.—Morton and Widger feel that it is unfortunate to limit the blood amylase test to a transient period in the severe hemorrhagic necrotic forms of pancreatitis. They suggest that blood should be taken for blood matching for transfusion, for the icteric index and for the amylase test. If perforated ulcer or obstruction is suspected roentgenograms may demonstrate free air in the abdominal cavity or they may show the obstructed loops. If these examinations reveal nothing significant, the amylase test may be helpful in arriving at the correct diagnosis. Abdominal paracentesis may be of assistance. An amylase test on fluid recovered by aspiration may be diagnostic. In the authors' cases in which the pancreas was drained the fluid gave high amylase test values. Acute pancreatic abscesses should be drained. The acute, fulminating, hemorrhagic, necrotic type has had a high mortality rate in the past

from immediate operation. Shock should be adequately treated and fluid balance restored in these cases. In the very ill patients the most simple surgical treatment should be undertaken. If jaundice is present, drainage of the gallbladder or common duct may be advantageous. The pancreas should be disturbed as little as possible, as it cannot be drained by splitting the capsule as formerly advocated. The drains should be placed against the surface of the pancreas after the peritoneum over it has been spread apart or incised. In the milder edematous form of acute pancreatitis the amylase test is most useful. This form of pancreatitis subsides in most instances. After the subsidence exploration of the common duct with drainage for some weeks is usually all that is necessary for cure.

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- Type Specific Antigenic Protein Derived from Staphylococcus. W. F. Verwey, New York.—p. 635.
- Infectivity and Immunity Resulting from Injection of Poliomyelitis Virus by Intracutaneous Route. F. D. Stimpert and J. F. Kessel, Los Angeles.—p. 645.
- Behavior of Pox Viruses in Respiratory Tract: III. Survival of Variola and Vaccinia Viruses in Lungs of Mice Previously Infected with Variola. J. B. Nelson, Princeton, N. J.—p. 653.
- Inactivation of Virus of Epidemic Influenza by Soaps. C. C. Stock and T. Francis Jr., New York.—p. 661.
- Avian Thiamine Deficiency: Correlation of Pathology and Clinical Behavior. R. L. Swank, Boston.—p. 683.
- Ultracentrifugation Studies of Yellow Fever Virus. E. G. Pickels and J. H. Bauer, New York.—p. 703.
- Dog Test for Measuring Immunizing Potency of Antirabies Vaccines. L. T. Webster and J. Casals, New York.—p. 719.

Journal of Urology, Baltimore

43:623-766 (May) 1940

- *Acute Staphylococcal Infections of Kidney. R. N. Nesbit and V. S. Dick, Ann Arbor, Mich.—p. 623.
- *Pelvic Lavage with Sulfanilamide in Treatment of Renal Infections. G. Austen Jr., Boston.—p. 637.
- Familial Tendency to Renal Carcinoma. P. Nowlin, Charlotte, N. C.—p. 654.
- Multilocular Cysts of Kidney: Report of Case. N. L. Burrell, Springfield, Ohio.—p. 656.
- Spontaneous Rupture of Hydronephrotic Kidney Associated with Primary Carcinoma of Ureter. H. J. Jewett, Baltimore.—p. 664.
- Pneumopyelography. J. B. Morgan, Cleveland.—p. 669.
- Retrocaval Ureter: Report of Case, with Discussion of Its Clinical Significance. J. W. Pick and B. J. Anson.—p. 672.
- Easy Method of Removing Large Diverticula of Bladder. E. L. Peirson, Salem, Mass.—p. 686.
- Urinary Retention from Imbalance of Detrusor and Vesical Neck: Treatment by Transurethral Resection. J. L. Emmett, Rochester, Minn.—p. 692.
- Effect of Castration on Benign Hypertrophy of Prostate in Man. C. Huggins and R. A. Stevens, Chicago.—p. 705.
- Acute Appendicitis with Abdominal Abscess Involving Undescended Abdominal Testicle: Report of Case. A. Lesser and J. G. Keshin, New York.—p. 715.
- Improved Continuous Flow Recording Cystometer. D. K. Rose, St. Louis.—p. 718.
- Tortuous Urethra: Method of Threading for Catheterization. A. N. Collins, Duluth, Minn.—p. 720.
- Studies in Malignant Tumors of Testis: I. Differential Diagnosis of Clinically Obscure Tumors: Four Cases and Review of 122 from Literature. J. B. Gilbert, Schenectady, N. Y.—p. 722.
- Hematuria: Ureteral Clot 6 Feet Long in a Case of Lymphosarcoma. P. O. Hageman, St. Louis.—p. 734.
- *Treatment of Gonorrheal Arthritis: Analysis of 200 Cases. O. S. Culp, Baltimore.—p. 737.

Staphylococcal Infections of Kidney.—Nesbit and Dick state that certain features of acute staphylococcal infections of the kidney tend to obscure its early diagnosis. The condition is frequently not recognized and its complications—perinephric abscess and renal carbuncle—are rarely diagnosed until they have been present for some time. Eighty such cases seen at the University Hospital are discussed. The cases presented no apparent preexisting infection of the urinary tract and were uncomplicated by obstructive lesions. The route of infection is hematogenous. *Staphylococcus aureus* is the most frequent invading organism, although any of the other strains of staphylococcus may be responsible. The port of entry is the skin or mucous membranes. Furuncles and carbuncles are the most common cutaneous foci, while infections of the upper respiratory tract are the most frequent mucosal precursors. In many instances no primary lesion can be demonstrated, suggesting that the port of bacterial invasion may be insignificant. The kidney is enlarged and multiple small areas of suppuration are disseminated throughout the cortex. The more extensive suppurative processes, which occur rarely, have been described as "abscess of the kidney," "septic infarct" and "renal carbuncle." The lesions heal rapidly unless extensive suppuration occurs. In all but seven of the eighty cases the onset was abrupt. Costovertebral pain of moderate severity, constant and aching, was

present from the onset in all but three. If extremely severe, it simulated renal colic. Loss of appetite, malaise, general weakness, occasionally prostration and rarely nausea and vomiting were present. Chills occurred in forty-six. The average temperature was 102 F. Leukocytosis was constant. Staphylococci are demonstrated in the urine by staining the centrifuged sediment. Their rapid disappearance has often led to confusion in diagnosis not only of simple coccic renal infection but also of its serious complications. Secondary invasion by the colon bacillus occurred from the seventh to the tenth day and persisted longer than the primary invader in twenty-nine of the eighty cases. With this invasion pus cells always appeared in the urine. The diagnosis is made without difficulty, except in rare instances in which the urine fails to show cocci for the first few days. In these cases costovertebral tenderness, fever and leukocytosis are diagnostic. Failure of diagnosis is generally due to failure to suspect the disease. The lesion most commonly confused with this condition is acute appendicitis, but the absence of nausea, vomiting and muscle spasm, with the presence of costovertebral tenderness and high leukocytosis, should be sufficient for differentiation. Acute hydronephrosis and cholecystitis must be ruled out. Uncomplicated staphylococcal renal infections run a stormy course the first week, followed by improvement of all symptoms and signs. Usually by the fourteenth day the temperature returns to normal and the patient is free from pain or tenderness. If symptoms and signs fail to subside or are accentuated, one of the surgical complications must be suspected. Uncomplicated cases end in complete recovery, except for cortical scars, which probably have no bearing on renal function. Patients with surprisingly serious infections without complications recover quite rapidly without operation. The nine patients with renal carbuncle were treated by operation; nephrectomy was performed on one and simple drainage on the others, with eventual complete healing in each instance. The forty-eight patients with perinephric abscess were all treated by incision and drainage. There were no postoperative deaths and no secondary nephrectomies. All pulmonary complications of renal or perirenal suppuration cleared up promptly on adequate surgical drainage of the subdiaphragmatic primary lesion.

Pelvic Lavage with Sulfanilamide for Renal Infections.—Austen administered sulfanilamide directly to ten patients with infections of the upper part of the urinary tract. These patients either did not tolerate the drug well or it was unwise to administer it by the usual routes because of anemia, granulocytopenia, diminished renal function, or the presence of an anatomic or pathologic abnormality preventing high local concentration or because there was interference with renal drainage. The drug administered by direct pelvic instillation was well tolerated by all except one patient. A definite clinical and bacteriologic improvement was observed in eight cases, a bacteriologic cure in one and no improvement in one. Observations on the concentration of sulfanilamide in the blood, in the urine from the injected kidney and in the urine from the uninjected kidney demonstrated that the drug was absorbed from the renal pelvis into the blood stream in appreciable amounts and that it was also excreted in the urine from the uninjected kidney. The concentration of sulfanilamide in the urine from the injected kidney reaches a much higher level than is possible when the drug is administered by the oral or subcutaneous routes. The author feels that although the method has definite limitations the direct pelvic instillation of sulfanilamide is a worth while procedure in the treatment of selected cases of renal infection.

Treatment of Gonorrheal Arthritis.—Culp evaluates the efficacy of various therapeutic measures employed at the Johns Hopkins Hospital in the treatment of gonorrheal arthritis during the last twenty years. The unimpaired function of the joint as the end result was the chief criterion used. Only those cases in which there was no doubt about the true etiology of the arthritis were included. They have been unselected otherwise. Forty-five of the cases were chronic, fifty subacute and 105 acute. Of the methods employed, sulfanilamide, intravenous injections of mercurochrome and fever therapy gave the best results. Of twenty-nine patients treated with intravenous injections of mercurochrome 69 per cent were discharged as being

well or markedly improved. Excellent results were obtained in cases of chronic, subacute and acute involvement. Only 53 per cent of the nineteen patients given fever therapy were well or markedly improved. Most of these were given only one session of fever. Several patients had severe reactions, and one died while undergoing treatment. Cures were effected in the chronic as well as in the earlier cases. Of the twenty-two patients treated with sulfanilamide 68 per cent left the hospital well or markedly improved. Most of the cases were acute and showed amazing improvement despite bone changes in a few instances. Results were less striking in cases of subacute and chronic involvement. Chemotherapy appears to be more efficacious than any other treatment. Sulfanilamide and intravenous injections of mercurochrome are recommended for the routine treatment of gonorrheal arthritis and seem to be of about equal therapeutic value. Both often result in surprisingly rapid cures. The thirty-four patients whose treatment was limited to bed rest and sedatives did poorly. Baking, diathermy, massage, prostatic massage and passive motion failed to cure any of the forty-nine patients. Poor results were obtained in the remaining forty-one cases with aspiration and the injection of air, hot compresses, manipulation under anesthesia, immobilization, incision and drainage or vaccines (typhoid or antigenococcus).

Kentucky Medical Journal, Bowling Green

38:187-230 (May) 1940

- Newer Concepts of Allergy. M. B. Cohen, Cleveland.—p. 188.
Diagnosis of Allergic Conditions. F. A. Simon, Louisville.—p. 190.
Treatment of More Common Allergic Diseases. A. E. Cohen, Louisville.—p. 193.
Allergy in Dermatology. A. B. Loveman, Louisville.—p. 195.
The Management of the Allergic Child. I. Rosenbaum Jr., Louisville.—p. 199.
Treatment of Pneumonia in Children with Sulfapyridine. W. W. Nicholson, Louisville.—p. 203.
Rupture of Urinary Bladder. N. L. Bosworth, Lexington.—p. 206.
Differential Diagnosis of Acute Exanthems. C. C. Carroll, White Mills.—p. 209.
Hemorrhoids: Local and Systemic Considerations. R. C. Alley, Lexington.—p. 212.
Etiology and Management of Posterior Position. W. Hord, Maysville.—p. 215.
Swine Erysipelas in Man. D. L. Jones, Fulton.—p. 218.
Anemia as a Problem for the Pediatrician. H. Gordon, Louisville.—p. 222.
Tuberculous Meningitis: Report of Case. H. G. Wells, Georgetown.—p. 224.

Medical Annals of District of Columbia, Washington

9:153-188 (May) 1940

- Sulfapyridine: Its Nature and Some Theories of Its Action. G. B. Roth, Washington.—p. 153.
Clinical Use of Sulfathiazole in Pneumonia. T. J. Abernethy, Washington.—p. 159.
"Vascular Headache": Report of Case Successfully Treated with Histamine. W. M. Yater, Washington.—p. 165.
The New Law for the Commitment of the Mentally Ill. R. S. Cohen, Washington.—p. 167.
Granuloma Resulting from Penetration of Talcum Powder: Report of Case. E. de Savitsch, Washington.—p. 169.

Minnesota Medicine, St. Paul

23:311-382 (May) 1940

- *Gastroscopic Observations in Pernicious Anemia. J. B. Carey, Minneapolis.—p. 311.
Proper and Adequate Protein Diet for Elderly People. E. L. Tuohy, Duluth.—p. 313.
Genital Tuberculosis. G. J. Thomas, T. L. Stebbins, Minneapolis, and F. J. Rigos, Oak Terrace.—p. 318.
Surgical Drainage of Abdomen: Review of Literature. R. A. Glabe, Plainview.—p. 323.
Management of Acute Abdominal Emergencies. J. M. Waugh, Rochester.—p. 331.
Treatment of Mental Defectives in Minnesota. E. J. Engberg, Faribault.—p. 335.
Present Day Treatment of Ununited Fractures of Neck of Femur. M. S. Henderson, Rochester.—p. 339.
Surgery of Common and Hepatic Duct Calculi. H. Mattson, Minneapolis.—p. 344.
*Fulminating Ulcerative Colitis: Critical Analysis of Twenty Cases. C. P. Schlicke and J. A. Barga, Rochester.—p. 348.

Gastroscopic Observations in Pernicious Anemia.—

According to Carey, many patients with pernicious anemia have been examined gastroscopically and the presence of an atrophy of greater or lesser degree has been noted. Whether this con-

dition is amenable to adequate liver therapy has been discussed, and favorable and unfavorable results have been recorded. The author has not seen an indubitable case of pernicious anemia with a normal gastric mucosa in the course of 750 examinations. He has not seen restoration to a normal condition of the gastric mucosa in any of the patients reexamined after treatment, although in some cases some evidence of regeneration was present. Of fifteen patients in whom the diagnosis of pernicious anemia had been made on the basis of all the accepted criteria, six were reexamined and still showed atrophic mucosa, although in two there was some improvement in that there were present what were thought to be areas of regeneration. One was definitely worse in that the atrophy was more extensive, and three were unchanged. The author points out that the reversion to a normal condition of the gastric mucosa in pernicious anemia patients treated with liver would be contrary to the pathologic and histologic studies of Meulengracht and Faber. Both of these authors have examined postmortem material from pernicious anemia patients adequately controlled as to anemia and dying from intercurrent causes and have always found an atrophic condition of the mucosa with gastritis. Changed conditions of general nutrition and blood elements brought about by liver therapy might conceivably result in some improvement in gross appearance of gastric mucosa as to color and even in the direction of recession of atrophic appearance. But in any gastritis the replacement of diseased gastric cells is by nonspecific, simple columnar epithelium and not by functional cells capable of secreting specific substances. This is in line with the experimental evidence that the hydrochloric acid does not return to the gastric secretion in pernicious anemia in spontaneous or induced remission, nor does the so-called intrinsic factor. If liver therapy actually restored the gastric mucosa to normal, the patient would be actually cured of his pernicious anemia. This happy result has, so far, not been accomplished.

Fulminating Ulcerative Colitis.—Schlicke and Barga state that approximately 300 cases of chronic ulcerative colitis have been seen at the Mayo Clinic during each of the last three years and that between five and seven patients have died from this disease annually. The cases selected for study represent the last ten in which the outcome was fatal. As a basis for comparison, an analysis was made of ten similar cases of fulminating ulcerative colitis, in which the patient recovered. This investigation represents an attempt to make a critical analysis of the factors contributing toward the mortality and of the value of the therapeutic efforts with an attempt to improve the management of similar cases in the future. Most of the patients were in the third or fourth decade of life. Nine of the twenty patients were Jews. The severity of the disease and the outcome bore no relation to the duration of the symptoms, the mode of onset, the type or extent of involvement of the colon at the time of admission or to the blood picture. The similarity in the course of the two groups of cases is emphasized by the fact that in each there were seven cases presenting severe sepsis and two or three presenting secondary deficiency states. Streptococci of colitis were recovered from the stools in all but one case in which the patient survived but in only two of the cases in which the patient died. In most cases the clinical picture and course were produced or, at least, influenced by the severity of the infective process, but in some a secondary deficiency state was the predominant feature. Perforation, jaundice and edema were the most serious complications. Perforation and peritonitis were the most common causes of death. No one drug or procedure is curative in "chronic ulcerative colitis" of this fulminating variety. A program including the use of serums and vaccine and embracing dietary and medicinal aids seems to be the best form of treatment. Each of the ten patients who survived received an adequate course of serum. Few of the ten who died received amounts of serum worthy of comment. Nine of the patients who survived received anticolitis vaccine as well. Only two of the patients who died received the vaccine. The use of sulfanilamide and azosulfamide in the treatment of chronic ulcerative colitis is still in a trial stage. Although of proved value in many cases, their use is not entirely unattended by danger, especially in cases of the fulminating variety.

New England Journal of Medicine, Boston

222:783-826 (May 9) 1940

- Acute Appendicitis as Complication of Carcinoma of Cecum. M. K. Bartlett and R. H. Miller, Boston.—p. 783.
The National Health Act of 1939. R. B. Osgood, Boston.—p. 785.
*Prognostic Factors in Carcinoma of Breast. G. W. Taylor and N. H. Bruce, Boston.—p. 790.
*Antemortem Recognition of Pulmonary Embolism. A. S. Johnson, Springfield, Mass.—p. 793.
Otolaryngology. C. G. Flake, Boston.—p. 796.

222:827-864 (May 16) 1940

- Fractions of Carpal Scaphoid. A. Thorndike Jr. and W. E. Garrey, Boston.—p. 827.
Changes in Public Health Practice. C. F. Wilinsky, Boston.—p. 831.
Fever Therapy in Allergic Disease. R. W. Hyde, Fairfax, Vt.—p. 839.

Prognostic Factors in Carcinoma of Breast.—According to Taylor and Bruce, in a considerable number of cases of carcinoma of the breast, operable by the usual criteria and subjected to radical mastectomy, early recurrence of the disease develops and runs a rapidly fatal course. In an effort to discover factors common to these cases and possibly of prognostic value, the authors have studied a group of thirty patients, all of whom had received radical mastectomy, with subsequent rapid recurrence and death within eighteen months. For comparison, two other similarly treated groups were studied. One of these consisted of forty-eight patients who had died of recurrence after eighteen months, while the other was made up of forty-seven patients living and well five or more years after the radical mastectomy. These groups were investigated with regard to such factors as preoperative duration, size and location of lesion, cutaneous involvement and axillary involvement. The preoperative duration was shorter and the size of the lesion smaller in cured cases. Large lesions and those with cutaneous involvement or extensive axillary involvement offer a poor prognosis, in many cases so poor as to contraindicate surgical intervention even in the absence of remote metastases. The operative risk must be given careful consideration. Old age, obesity and hypertension seem to increase the hazard. While it is still impossible to prognosticate accurately in any single borderline case, the authors believe that the chance of cure should be carefully weighed against the operative risk and the normal life expectancy. Palliative measures may well be indicated more often than they are now employed.

Antemortem Recognition of Pulmonary Embolism.

Johnson thinks that the unanimity of opinion as to the diagnostic criteria for pulmonary embolism should render an accurate diagnosis a simple matter. A study of forty-three fatal cases in which necropsy showed pulmonary embolism to have been the immediate cause of death revealed that only three cases answered the description of pulmonary embolism. In nine cases the clinical picture was so atypical as to make the diagnosis of pulmonary embolism unwarranted, even in retrospect. Furthermore, the author encountered a significant number of patients who presented a sufficient number of these criteria ante mortem to warrant a diagnosis of pulmonary embolism but in whom the pathologist found sepsis, without evidence of embolism, as the cause of death. This study was undertaken in order to reappraise the validity of accepted diagnostic criteria. The author reviews observations on the forty-three cases and compares them with those of other investigators. He presents histories of nine cases in which the picture was so bizarre that a clinical diagnosis of fatal pulmonary embolism seemed unjustified. Before any lifesaving form of therapy can be instituted the clinical diagnosis of pulmonary embolism must be made. In about two thirds of the fatal cases the patients survive long enough for the application of some remedial measure. The author emphasizes the frequency and seriousness of pulmonary embolism and suggests that its possibility should be considered in any case in which the patient is not doing well, even though he has undergone no operation and presents no signs of infection. Dyspnea, tachycardia and cyanosis are early and frequent signs. Although often accompanied by collapse, this feature may be absent or may occur alone. There appears to be no single criterion short of necropsy by which the diagnosis of pulmonary embolism can be infallibly established or

excluded. It is believed, however, that if it is remembered that this condition can mimic, and be mimicked by, coronary thrombosis, bronchopneumonia, sepsis and surgical shock, greater diagnostic acumen will be developed.

New York State Journal of Medicine, New York

40:693-762 (May 1) 1940

- Cesarean Section: Ten Year Study Conducted in Rochester and Monroe County by the Committee on Maternal Welfare of the Medical Society of the County of Monroe. J. K. Quigley, Rochester.—p. 699.
Role of Infection in Sudden Death. J. R. Lisa and J. F. Hart, New York.—p. 705.
Preliminary Report on Activated Ergosterol: Form of High Dosage Vitamin D in Treatment of Chronic Arthritis. R. G. Snyder and W. H. Squires, New York.—p. 708.
Clinical Report on Eye Lesions Due to Nasal Sinus Infection. F. Barber and J. J. McNamara, Rochester.—p. 720.
Dermatitis Nodularis Necrotica: Report of Three Cases. E. T. Bernstein, New York.—p. 727.
Benign Intraventricular Tumors of Brain: Report of Three Cases. E. Campbell Jr. and R. Whitfield, Albany.—p. 733.
Milk: Role of Medical Milk Commissions in Developing Standards for Milk Production. E. S. Rimer, New York.—p. 741.
*Toxic Manifestations of Sulfapyridine. S. Katz, Newark, N. J.—p. 746.

Toxic Manifestations of Sulfapyridine.—Katz studied 100 consecutive patients for toxic manifestations of sulfapyridine. All symptoms and signs referable to toxicity were carefully recorded. Approximately one half of the adults and one fifth of the children exhibited some toxic side reactions. Nausea and vomiting, appearing in 25 per cent, were the most commonly encountered toxic manifestations. There was no apparent correlation between the gastric irritability and the amount of the drug administered. Disturbances of the central nervous system were observed in 7 per cent and varied from mild personality changes to the more serious psychoses. There were four cases of hematuria. This disturbance is apparently caused by the irritating effect of the sharp acetylsulfapyridine crystals that precipitate in the urine. Stasis appears to be an important predisposing factor in the production of hematuria following the use of sulfapyridine. Dermatitis in two cases and jaundice in three were the other serious symptoms noted. Diarrhea, lethargy, abdominal pain, cyanosis and dyspnea were also encountered. Drug fever, vertigo, headache, tingling of the extremities, acute hemolytic anemia and granulocytopenia were not observed. With the recognition of the toxic manifestations constant observation will allow detection of the toxic symptoms while they are amenable to appropriate countermeasures permitting this valuable drug to be used with a satisfactory margin of safety.

40:763-836 (May 15) 1940

- Biliary Duct Stones. P. Vayo and L. F. Simpson, Rochester.—p. 769.
Infections of Neck. A. G. Swift, Syracuse.—p. 779.
*Carcinoma of Breast. L. C. Kress, W. T. Murphy and E. M. Burke, Buffalo.—p. 787.
The New York Diabetic Association: Summer Camp for Underprivileged Diabetic Children. F. W. Williams and J. F. Hart, New York.—p. 795.
Postcaval Ureter. F. O. Harbach, Syracuse.—p. 800.
Use of Calcium Chloride in Treatment of Cbilds. P. B. Beeson and C. L. Hoagland, New York.—p. 803.
Pathology of Experimentally Produced Pulmonary Tuberculosis in Rabbit: Effect of Prophylactic Vaccination. E. M. Medlar and K. T. Sasano, Mount McGregor.—p. 805.
Toxemia of Pregnancy. M. B. Strauss, Boston.—p. 810.

Carcinoma of Breast.—Kress and his associates present their impressions gained over a period of four years from a study of 129 patients with cancer of the breast who received preoperative irradiation. All these tumors were proved malignant by aspiration biopsy, by careful removal of a small piece of the tumor or by operation. Preoperative irradiation was not instituted until a definite diagnosis was made. None of the patients were less than 30 years of age; the predominating age group was between 40 to 70. Carcinomas were equally frequent in the two breasts. The most common site was the upper outer quadrant of the breast. A lump was the principal first symptom and pain was next. Most of the lumps were discovered by the patient. The physician does not have the opportunity to detect early cancer, as patients do not generally have periodic health examinations. Delay from the discovery of the first symptom to medical consultation averaged 9.28 months. Popular cancer education is the solution for this delay.

The value of preoperative irradiation is questionable. It cannot replace surgery. Preoperative irradiation rendered 19 per cent of the tumors sterile. Very few axillary glands were sterilized by preoperative irradiation. Swelling of the arm and delayed union were encountered more often when preoperative irradiation was used. The most suitable interval between irradiation and surgery is eight weeks. The large cell tumor was found to be more sensitive to irradiation, the small cell was the least, and the sensitivity of the adenocarcinoma lay between these two groups.

Oklahoma State Medical Assn. Journal, Oklahoma City

33:1-58 (May) 1940

- Renal Tumors of the Wilms Type. H. S. Browne, Tulsa.—p. 6.
- Use of Vitallium Screws in Fractures of Long Bones. F. A. Stuart, Tulsa.—p. 8.
- Some Recent Advances in Ophthalmology. J. R. Reed, Oklahoma City.—p. 12.
- Résumé of Advance Made in Treatment of Human Pellagra, with Observation Made on Fifty Cases Treated with Nicotinic Acid and Whole Yeast Compounds. V. H. Musick, Oklahoma City.—p. 13.
- Anesthesia and Analgesia in Obstetrics and Its Relation to Asphyxia Neonatorum. R. J. Reichert, Moore.—p. 17.

Pennsylvania Medical Journal, Harrisburg

43:1057-1248 (May) 1940

- Relationship of Urticaria and Angioneurotic Edema to General Medicine. W. L. Winkenwerder, Baltimore.—p. 1073.
- Acroderosis. L. Hollander and H. R. Vogel, Pittsburgh.—p. 1089.
- Spreading Peritonitis: Its Prevention and Treatment. W. W. Babcock, Philadelphia.—p. 1093.
- *Use of Sulfanilamide in Treatment of Peritonitis of Appendical Origin. I. S. Ravdin, J. S. Lockwood and J. E. Rhoads, Philadelphia.—p. 1100.
- Surgical Treatment of Dislocated Lens. W. S. Reese, Philadelphia.—p. 1104.
- Salt and Water Balance and Acid-Base Equilibrium: Body Water and Electrolyte Control: General Application. C. G. Grosscup, Abington.—p. 1106.
- Id.: In Renal Disease. G. M. Piersol, Philadelphia.—p. 1111.
- Id.: The Problem of Water Balance in Congestive Heart Failure. W. D. Stroud and J. B. Vander Veer, Philadelphia.—p. 1116.
- Id.: Surgical Applications of Principles of Salt and Water Balance. D. B. Pfeiffer, Philadelphia.—p. 1121.
- Complicating Factors Following Open Reduction of Simple Fractures. D. C. Geist, Philadelphia.—p. 1126.
- Acute Laryngotracheobronchitis. F. W. Davison, Danville.—p. 1129.
- Lung Abscess. H. A. Kipp, Pittsburgh.—p. 1134.
- Pollen Asthma and Hay Fever in Children. S. C. Copeland and J. P. Keating, Philadelphia.—p. 1137.
- Progress Report from Division of Cancer Control of the Department of Health of the Commonwealth of Pennsylvania. S. P. Reimann, Philadelphia.—p. 1141.

Sulfanilamide for Peritonitis of Appendical Origin.—Ravdin and his associates point out that the mortality among 552 patients operated on for acute appendicitis with abscess or acute appendicitis with peritonitis prior to 1936 was 1.4 per cent. This includes one patient, nearly moribund on admission, who was not operated on. In this group are included only those patients with a pathologic report of acute diffuse suppurative appendicitis or worse. In 1936 the authors added the parenteral administration of sulfanilamide to their regular regimen. Since then and up to Sept. 1, 1939, 286 patients with acute appendicitis and acute appendicitis with abscess or varying degrees of peritonitis have been operated on, with a mortality of 0.3 per cent. The only death which occurred was of a patient who had an acutely inflamed appendix but little evidence of peritonitis. Sulfanilamide was begun two days after operation when evidences of a widespread peritoneal infection were apparent. Necropsy disclosed a leaking appendical stump. Although the reduction in mortality does not appear to be great, the authors are convinced that a number of lives of desperately sick patients have been saved by the administration of sulfanilamide during the postoperative period. Drainage is necessary in many instances. It has been used in 38 per cent of the 838 cases. The McBurney incision permits the placing of drains in contact with the parietal peritoneum so that intestinal obstruction is minimized. Ilcostomy has been necessary only once since the routine use of suction drainage in 1933. In nearly every instance the sulfanilamide has been given by hypodermoclysis. The crystalline sulfanilamide (Merck) was used. It was used preoperatively in cases of appendical abscess so as to minimize spread of the infection if transperitoneal drainage became neces-

sary. The total dosage given has been approximately 8 Gm. the first day, the amount being gradually reduced to 3 Gm. in from four to six days, at which time if the patient was doing well the drug was discontinued. The daily dosage is given in from four to six doses. The blood concentration of sulfanilamide has been maintained above 5 mg. per hundred cubic centimeters of blood, and in a few cases it was kept above 15 mg. Drug therapy was continued in all instances until peristalsis was reestablished, flatus was passed by the anus, abdominal relaxation had taken place and the temperature and pulse rate were returning to normal. No accessory method of treatment can take the place of early operation and skilful surgery, but late operation is often necessary and it is in such cases of desperate illness that accessory therapeutic agents can help reduce the mortality.

Public Health Reports, Washington, D. C.

55:861-914 (May 17) 1940

- Duration of Illness from Specific Diseases Among 9,000 Families, Based on Nationwide Periodic Canvasses, 1928-1931. S. D. Collins.—p. 861.
- Some Developments in Water Pollution Research Program of the Public Health Service. J. K. Hoskins.—p. 893.
- Viability of *Aedes Aegypti* Eggs. J. H. Le Van.—p. 900.

Radiology, Syracuse, N. Y.

34:521-650 (May) 1940

- Tuberculous Hilar and Mediastinal Adenopathy in Adults. B. P. Widmann, H. W. Ostrum and J. S. Fetter, Philadelphia.—p. 521.
- Intractable Heartburn of Pregnancy. J. R. Evans and J. S. Bouslog, Denver.—p. 530.
- Why the Film Size? R. A. Rendich and L. A. Harrington, Brooklyn.—p. 536.
- Irradiation and Hereditary Mammary Cancer. S. E. Owen and A. E. Williams, Hines, Ill.—p. 541.
- Ileocecal Region. A. Oppenheimer, Beirut, Lebanon, Syria.—p. 545.
- Radium Protection: Measurements of Exposure to Gamma Rays. R. E. Fricke and M. M. D. Williams, Rochester, Minn.—p. 560.
- Cholecystography: Optimal Voltage: Tetrabromophenolphthalein versus Tetraiodophenolphthalein. R. R. Newell and R. Briggs, San Francisco.—p. 568.
- Protrusion of Appendical Stump Following Appendectomy. M. Feldman, Baltimore.—p. 571.
- Odontomas: Case Report. L. A. Malone, Terre Haute, Ind.—p. 573.
- Multiple Diverticula of Jejunum, Duodenum and Colon: Report of Case. S. Hatchette, Lake Charles, La.—p. 577.
- Recent Advances in Nuclear Physics. E. U. Condon, Pittsburgh.—p. 581.
- Lower Lobe Tuberculosis. M. J. Sokoloff, Philadelphia.—p. 589.
- *Group X-Ray Surveys in Apparently Healthy Individuals. A. B. Robins and D. E. Ehrlich, New York.—p. 595.
- Treatment of Carcinoma of Rectum by Electrocoagulation and Radiation in Selected Cases. H. I. Teperson, Brooklyn.—p. 610.
- Shellac Bezoars. H. H. Inlow, Shelbyville, Ind.—p. 618.
- Serial Plancography (Serioscopy) and Serial Planigraphy: Critical Analysis. J. Kaufman and H. Koster, Brooklyn.—p. 626.

Group X-Ray Surveys.—Robins and Ehrlich report the result of examining more than 73,000 apparently healthy individuals roentgenographed in a routine manner from January 1937 to September 1938. There were 14,177 high school children, 53,237 persons of the home relief population of Harlem, 3,643 homeless men and 2,500 prisoners committed for not longer than three years. Active tuberculosis was found in 0.4 per cent of the high school children. The incidence of 3.1 per cent of active pulmonary tuberculosis in the home relief population is in close agreement with results previously obtained in New York City. The highest incidence of active tuberculosis was obtained in the prisoners, 5.9 per cent of them showing significant lesions. Since the prison sentence of this population was short, the high rate of disease is to be attributed to the economic background and is not associated with the stay in the penal institution. Confirmatory evidence of the importance of economic status and its attendant living conditions on tuberculosis is evidenced by the 16.1 per cent incidence among the homeless men. The average age of this group of men was 50 years and they existed at a bare subsistence level. The tuberculosis of more than 5 per cent of these men was active. The incidence of active and arrested tuberculosis by age followed the expected pattern. The distribution of active pulmonary tuberculosis by age and sex closely paralleled the mortality curves for men and women in New York City. Contrary to accepted beliefs, the incidence of active tuberculosis in the Negro population of the groups was considerably lower than in the

white population. Only in the high school group was the rate in Negroes higher than in the white population. Most of the cases in the entire group were discovered in the minimal stage of tuberculosis. Abnormal cardiac outlines significant of organic disease of the heart or vessels were found in a sufficiently high percentage of cases to warrant the universal use of roentgenography. In rapid examinations of large groups, the roll-paper method is the procedure of choice from the point of view of convenience, accuracy and economy.

Southern Medical Journal, Birmingham, Ala.

33:449-558 (May) 1940. Partial Index

- *Local Implantation of Sulfanilamide in Compound Fractures: Its Effect on Healing. J. A. Key and T. H. Burford, St. Louis.—p. 449.
- Bilateral Renal and Ureteral Calculi. A. I. Folsom and H. A. O'Brien, Dallas, Texas.—p. 455.
- Chronic Leg Ulcerations in Congenital Hemolytic Jaundice. L. H. Leger and T. G. Orr, Kansas City, Kan.—p. 463.
- Chronic Female Pelvic Disease. R. J. Wilkinson, Huntington, W. Va.—p. 464.
- *Familial Benign Chronic Pemphigus: Report of Thirteen Cases in Four Generations of a Family and Report of Nine Additional Cases in Four Generations of a Family. Howard Hailey and Hugh Hailey, Atlanta, Ga.—p. 477.
- Roentgenologic Aid in Acute Infections of Lung and Their Sequelae. H. B. Mulholland, University, Va.—p. 482.
- *Prolonged Atelectasis of Both Foreign Body and Nonforeign Body Origin: Bronchiectasis as End Result and Its Prevention by Bronchoscopic Care. V. K. Hart, Charlotte, N. C.—p. 487.
- Glaucoma Errors That I Have Made and That I Have Seen. H. S. Gradle, Chicago.—p. 498.
- Thyroid Anesthesia: Comparative Study. H. E. Doudna and G. S. Mechling, Oklahoma City.—p. 502.
- Public Health Aspects of the Trichinosis Problem in the South. K. B. Kerr, Washington, D. C.—p. 511.
- Prophylaxis of Malaria. H. Beckman, Milwaukee.—p. 516.
- Acute Anterior Poliomyelitis in South Carolina in 1939. W. Weston Jr., Columbia, S. C.—p. 525.
- Method for Initiating Respiration in the Newborn. N. Bograd, Montgomery, Ala.—p. 531.

Local Implantation of Sulfanilamide in Compound Fractures.—Key and Burford determined the effect of local implantation of crystals of sulfanilamide in experimental contaminated fracture wounds in rabbits and dogs. They found that such implantation did not retard the union of the experimental fracture of one foreleg when compared with the degree of union present in a similar fracture in the other foreleg. Local implantation of sulfanilamide crystals in compound fractures not only tends to lessen the danger of infection but does not perceptibly interfere with the union of the soft tissues or of the bone. However, such implantation does not permit the closing of grossly contaminated or infected wounds. The wound must be debrided in the usual way and all foreign material and devitalized tissue removed before the infection has gained a foothold and invaded the tissues, preferably within twelve hours after the injury. After the débridement and reduction of the fracture, the skin and subcutaneous tissues are sutured with a single layer of silkworm gut without drainage in order to retain the serum which is saturated with sulfanilamide. The authors believe that postoperative immobilization is an important factor in the prevention of infection. The upper limits of the method are not known but its routine use will enable the average surgeon to close with impunity most compound fractures. This is important not only in civil life but even more so in military surgery. Had the casualty wounds during the war of 1914-1918 been rapidly debrided, sprinkled with sulfanilamide crystals, sutured and the reduced fractures immobilized in casts or splints, the large majority of them would have stayed closed without infection and the soldiers could have been sent directly back to America from the casualty clearing station or field hospital. The method would have brought about a great saving in hospital personnel and materials and the effect on the morale of the soldiers would have been unlimited. The method is recommended in clean operations in which the development of an infection is feared; that is, operations involving tissues previously infected and in which the infection apparently has disappeared. Good results have also been obtained in the wounds of amputation stumps when the operation was done for gangrene and infection.

Familial Benign Chronic Pemphigus.—The Haileys add twenty-two cases of familial benign chronic pemphigus to their four previously reported cases. The cases occurred in four

generations of two families. The disease is familial and hereditary but not congenital. It is most likely to appear in early adult life and follow a chronic course over a period of years, with frequent recurrences and varying periods of freedom from the eruption. Toward late life the severity and frequency of the attacks are reduced. The disease is benign. There are no constitutional signs and symptoms and the disease does not appear to shorten the span of life. Pruritus or burning may be present. Tender regional lymph nodes are not constant. The primary lesion is a vesicle or a bulla arising on apparently normal skin. Nikolsky's sign (the skin is easily rubbed off) is present. Temporary pigmentation marks the site of recently healed lesions. Scarring never occurs. The lesions have a predilection for the neck, flexures and apposing cutaneous surfaces. Mucous membranes may be attacked. Treatment does not influence the course of the disease. Mild antiseptic wet dressings in the moist and early stage of the disease are palliative and discourage secondary infection. Boric acid ointment with 1 per cent ammoniated mercury on gauze makes a soothing dressing for the dry stage of the eruption. The authors state that their first report of the condition is substantiated by the present work. A number of authorities have observed similar cases and agree that another dermatologic entity, familial benign chronic pemphigus, has been identified.

Prolonged Atelectasis.—Hart emphasizes that prolonged atelectasis is the frequent forerunner of bronchiectasis. Therefore adequate drainage, particularly by bronchoscopy, is important. Nearly all bronchiectasis is acquired, much of it in childhood. Congenital bronchiectasis is rare. A congenital atelectasis is more probable with a subsequent bronchiectasis. There is increasing clinical and experimental evidence that atelectasis is the preceding and predisposing cause of bronchiectasis. The duration of atelectasis regardless of cause before bronchoscopic drainage is undertaken determines the rapidity of cure and the degree of future bronchiectasis. The sooner bronchoscopic care is undertaken, the greater the rapidity of cure and the number of recoveries. Conversely, the longer bronchoscopy is deferred the smaller the number of recoveries and the possibility of bronchiectasis as an end result is increased. Bronchiectasis is assumed to date from some acute illness of the respiratory tract with obstruction and infection as the dominant factors. Three things may happen: resolution without chronic changes, acute bronchiectasis or a potential bronchiectatic condition. The latter, if unchecked, may progress successively to early or more advanced cylindrical or saccular bronchiectasis or a combination of the two. Once bronchiectasis is established there is no cure but radical surgery, and this can be done only in selected cases. This further emphasizes the importance of prophylactic bronchoscopic care. The author purposely limits his case reports to children. Together with other bronchoscopists, he feels that this group represents the largest and most fertile field for prophylactic bronchoscopic care. Typical atelectasis is occasionally produced by abnormal tissue in the bronchus. In a child, this is usually not malignant and in the absence of a foreign body is probably most commonly produced by the erosion of the bronchial wall by a tuberculous lymph node, with the production of granulation tissue. The same may occur in an adult. Early bronchoscopic removal is definitely indicated. A healed bronchial stricture should likewise be treated bronchoscopically by dilatation if obstruction and atelectasis ensue.

Tennessee State Medical Assn. Journal, Nashville

33:159-196 (May) 1940

- An American Health Program. N. B. Van Etten, New York.—p. 159.
- Why Medicine? W. O. Baird, Henderson.—p. 168.

Wisconsin Medical Journal, Madison

39:337-412 (May) 1940

- Adequate Diet in Later Life. E. L. Tuohy, Duluth, Minn.—p. 353.
- Observations on Use of Sulfapyridine. T. E. Gundersen, La Crosse, and M. Friedman, Kansas City, Mo.—p. 360.
- Persistent Enuresis. A. J. Hood and B. B. Madison, Milwaukee.—p. 363.
- Thrombophlebitis in Obstetrics. A. M. Lindner, Racine.—p. 368.
- Nonsuppurative Disease of Cornea. E. R. Ryan, Milwaukee.—p. 372.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

52:141-172 (May) 1940

Cancer of Skin. H. MacCormac.—p. 141.
Dermatitis from 9-Bromofluorene and Peculiar Reaction to Patch Test: Case. A. Cavendish.—p. 155.

British Journal of Ophthalmology, London

24:201-264 (May) 1940

The Fundus and Fovea Centralis of Albatross (*Diomedea Cauta Cauta*—Gould). K. O'Day.—p. 201.
Spasm of Branch of Central Artery: Personal Experience. H. Grimsdale.—p. 208.
Mycetoma of Eyelid. J. S. Aldridge and R. Kirk.—p. 211.
Development of Ophthalmology in Bombay. J. N. Duggan and V. K. Chitnis.—p. 213.
Microphthalmia and Visual Pathways: Case Associated with Blindness and Imbecility, and Sex Linked. S. E. Whitnall and R. M. Norman.—p. 229.

British Medical Journal, London

1:757-798 (May 11) 1940

Recent Knowledge of Incidence and Control of Cerebrospinal Fever. E. A. Underwood.—p. 757.
Goiter in South Wales. I. J. Davies and L. Rogers.—p. 764.
Renal Threshold for Glucose: Normal and in Diabetics. R. D. Lawrence.—p. 766.
Prevention of Throat Infection. Helen Pixell Goodrich and G. L. Way.—p. 768.
*Congenital Complete Heart Block: Effect of Atropine: Case. G. M. Currie.—p. 769.

Congenital Complete Heart Block.—Currie reports a case of congenital complete heart block in a child of 2 admitted to the hospital with a probable diagnosis of meningitis or infantile convulsions. X-ray examination revealed enlargement of the heart due to congenital abnormality. Electrocardiograms, before and after the injection of atropine, showed that the drug failed to break the complete block. The effect of $\frac{1}{100}$ grain (0.00065 Gm.) of atropine was to raise the auricular rate out of all proportion to the rise in the ventricular rate; the latter fell much more quickly to its original rate than the auricular. Electrocardiograms eight months later still showed a complete block, the auricular rate being 124 a minute and the ventricular rate 36. Since the previous examination the parents, now instructed as to what to look for, had been able to describe several Stokes-Adams attacks, lasting a few minutes at the most. Otherwise the child had been well and had played about normally. The case is one in which atropine affected the ventricular rate in spite of the complete block cutting off action through nerve control. On another occasion, after the injection of 3 minims (0.2 cc.) of epinephrine the ventricular rate rose to 48, the block still remaining complete. In view of the clinical observations, the compliance with Yater's postulates, the x-ray study and the electrocardiograms, this is undoubtedly a case of congenital complete heart block, associated with probable patent interventricular septum and Stokes-Adams attacks.

Indian Medical Gazette, Calcutta

75:129-192 (March) 1940

Aortic Stenosis. G. Kelly.—p. 129.
*Observations on Use of Nicotinic Acid in Treatment of Pellagra and Allied Conditions. J. W. D. Goodall.—p. 147.
Experience with Diseases of Gallbladder. V. M. Kaikini.—p. 153.
Adult of Microfilaria Malayi Brug, 1927. S. Sundar Rao and P. A. Mapleston.—p. 159.
Simple and Inexpensive Flea-Proof Cage. C. L. Pasricha and G. Panja.—p. 160.
Topical Application of Sulfanilamides. A. C. Dey.—p. 161.

Nicotinic Acid for Pellagra and Allied Conditions.—Goodall used nicotinic acid in the treatment of three cases of true pellagra, twelve of nicotinic acid deficiency and miscellaneous cases of allied conditions. Nicotinic acid was given in varying dosages according to the severity of the case. Of the twenty patients, eleven were cured, seven were improved, one did not finish the course of treatment and one obtained no improvement. The author states that although pellagra is quite a common disease in Bengal there is a much larger group of

cases of nicotinic acid deficiency, especially among Anglo-Indians, showing such symptoms as sore tongue, anorexia, stomatitis, diarrhea and mental dulness, which respond well to nicotinic acid therapy. Certain cutaneous conditions, such as infected scabies, show improvement with nicotinic acid therapy because this medication increases the blood supply of the affected area.

75:193-256 (April) 1940. Partial Index

Comparison of Thymol and Some Other Drugs in Treatment of Hookworm Infection. P. A. Mapleston and A. K. Mukerji.—p. 193.
Haffkinine (Acridine), an Atabrine-like Compound Prepared in India, in Indian Strains of Malaria. R. N. Chopra, R. T. M. Hayter and B. Sen.—p. 200.
Crimodora (Palusan) in Indian Strains of Malaria. R. N. Chopra, R. T. M. Hayter, B. Sen and M. Talukdar.—p. 202.
Typhus Fever in Bombay. T. B. Patel.—p. 208.
Miniature Mass Radiography (Plea for Its Adoption). S. C. Roy.—p. 209.
Role of X-Ray Screening in Detecting Pulmonary Tuberculosis. K. Eisenstaedt and A. U. Rindani.—p. 210.
Destruction of Air-Borne Bacteria. R. C. Wats and G. K. Kamat.—p. 212.
Role of Calcic Fumigation as Raticidal and Pulicidal Measure in Anti-plague Campaign. C. L. Ahluwalia.—p. 219.
Note on Production of Agglutinins in Blood of Individuals After Peroral and Subcutaneous Vaccination by Typhoid and Paratyphoid Vaccines. E. Somasekhar.—p. 223.

Journal of Mental Science, London

86:341-590 (May) 1940

Morgagni's Syndrome: Clinical and Pathologic Study. R. E. Hemphill and E. Stengel.—p. 341.
Contribution of Rorschach Method to Wartime Psychologic Problems. M. R. Harrower-Erickson.—p. 366.
Prognosis in Schizophrenia. D. Blair.—p. 378.
Adaptiveness and Equilibrium. W. R. Ashby.—p. 478.
Has Fear Any Therapeutic Significance in Convulsion Therapy? L. C. Cook.—p. 484.
Some Observations on Psychologic Aspects of Cardiazol Therapy. R. Good.—p. 491.
Influence of Cardiazol on Chronic Schizophrenia. A. J. Bain.—p. 502.
Relationship Between Disturbance of Liver Function and Mental Disease. P. Berkenau.—p. 514.
Prolonged Narcosis with Paraldehyde and Dial. M. B. Brody.—p. 526.
Note on Use of the 1937 Revision of Stanford Binet Vocabulary List in Mental Hospital Patients. M. B. Brody.—p. 532.
Ascorbic Acid Levels in Patients Suffering from Psychoses of Senium. D. G. Remp, S. R. Rosen, J. B. Ziegler and D. E. Cameron.—p. 534.

Lancet, London

1:865-910 (May 11) 1940

Laboratory Diagnosis of Diphtheria: Comparative Values of Various Mediums. K. E. Cooper, F. C. Happold, K. I. Johnstone, J. W. McLeod, H. E. de C. Woodcock and K. S. Zinnemann.—p. 865.
Death in the First Month and the First Year. C. McNeil.—p. 869.
*Follicular Hyperkeratosis: Sign of Malnutrition? J. Pemberton.—p. 871.
Hypertensive Effect of Blood from Hypertensive Dogs. D. Y. Solandt, R. Nassim and C. R. Cowan.—p. 873.
Spontaneous Pneumothorax and Staphylococci Lung Abscess in an Infant. J. L. Collis and A. F. Foster-Carter.—p. 875.
Removal of Impacted Lower Wisdom Tooth. W. W. James.—p. 876.
Treatment of Dropsy with Mercurial Diuretics and Urea. M. Winternitz.—p. 879.

Follicular Hyperkeratosis.—The cutaneous eruption described by Pemberton was observed during a survey of the nutrition of adolescents, school children and children of pre-school age in different parts of Great Britain. The eruption consists of crops of enlarged hair follicles appearing first on the extensor aspects of the arms, legs and buttocks and later and less commonly over the scapulas, back and abdomen. The eruption is symmetrical and does not irritate. The skin feels dry and rough and is sometimes furfuraceous. The hair follicles are enlarged, firm and cone shaped. The hair is absent from many follicles, and in its place there projects a tiny spine of horny material. These spines account for the roughness or "nutmeg-grater skin." At the orifices of some of the follicles the hair can still be seen, often curled, shriveled or broken. Occasionally the follicle is mildly inflamed. Sometimes the enlarged follicle is surmounted by a flat imbricated scale instead of a horny spine. The sexes were equally affected but it was not seen in children under 5. The fully developed condition was present in about 5 per cent of 3,000 children. Simple enlargement of the hair follicles, resembling a permanent cutis anserina, on the extensor aspects of the arms and legs, without projection of horny spines from the orifices of the follicles, was

found in about 20 per cent of the children. In these cases the skin was not noticeably dry. The eruption tends to develop in several members of the same family. Microscopic examination showed hyperkeratosis of the hair follicles, absence of sebaceous glands and round cell infiltration round the follicles. It is thought that this eruption is similar to the follicular hyperkeratosis or phrynoderma described by various writers in Africa and the Far East and that it is of nutritional origin. The specific dietary deficiency to which follicular hyperkeratosis may be attributed has not been certainly established, but the condition is probably an early sign of a deficiency of vitamin A or of fat.

New Zealand Medical Journal, Wellington

39:63-116 (April) 1940

- *X-Ray Treatment of Carcinoma of Breast: Survey of Results. B. Mackenzie.—p. 66.
Goiter After Middle Age. R. Chisholm.—p. 74.
Physiologic Approach to Study of Hysteria. I. M. Allen.—p. 79.
Catheterization of Ejaculatory Ducts. C. M. Greenslade.—p. 88.
Conservative Surgical Treatment of Acute Salpingitis: Report of Two Cases. R. O'Regan.—p. 93.

Röntgen Treatment of Carcinoma of Breast.—Mackenzie treated 104 cases of mammary cancer from private practice with x-rays. A high proportion of these were advanced with postoperative metastases or with inoperable primary lesions, and many were referred for only palliative treatment. Forty-nine patients (47 per cent) are still living. The period of survival ranges from three months to sixteen years, with an average of 5.4 years from the initial symptom. The five year survival rate is 35 per cent dating from roentgen therapy and 47 per cent dating from operation, the difference being due to the time lapse between operation and roentgen treatment. The average duration of life among the dead was 3.5 years calculated from the date of operation and 2.1 years from roentgen treatment. The prognosis appears to be better when the interval between operation and roentgen treatment is short. The value of ovarian irradiation in premenopausal established breast cancer is shown. In women before the menopause the results of this treatment are frequently dramatic. Advanced multiple metastases in bone, lung and skin (and possibly elsewhere) may clinically disappear without any local treatment to the metastases. This disappearance is hastened by small local doses of radiation. The period of freedom from symptoms is much longer than after only local treatment and survivals of five and six years are now on record. In women past the menopause the prognosis is little if at all improved by ovarian irradiation. The inferences to be drawn are that there is a natural tendency for breast cancer cells to revert to nonmalignant tissues and that, on the assumption that x-rays act inhibitory, this tendency is prevented directly or indirectly by the presence in the system of a substance elaborated by the ovary. At the normal menopause the elaboration of this substance would appear to be taken over by other tissues, thus accounting for the absence of post-menopausal response to ovarian irradiation. A questionnaire addressed to nearly 200 women whom the author has treated with ovarian irradiation for menorrhagia and nonmalignant conditions in the last eighteen years has revealed only one case in which breast cancer has developed. The numbers are too small to base conclusions, but they support the contention that the incidence of breast cancer is less after ovarian irradiation. Because of the strikingly favorable influence on demonstrable gross metastases, the author advises artificial sterilization of all women with breast cancer before the menopause. Inhibition of ovarian activity has no demonstrable effect on cancers of other organs, with the possible exception of the uterus, where the satisfactory results of roentgen therapy may in part be accounted for by the results of ovarian irradiation.

Chinese Medical Journal, Peiping

57:201-300 (March) 1940

- Massive Amyloidosis of Both Adrenal Cortices: Clinical Syndrome with Pathologic Findings. I. Snapper and K. Y. Ch'in.—p. 201.
Quantitative Determination of Urinary Estrogens in Cases of Uterine Hemorrhage. Hazel Ai-Ch'ün Lin.—p. 216.
Transplantation of Established External Biliary Fistula into Duodenum: Report of Case. C. K. Chi.—p. 231.
Acute Monocytic Leukemia: Report of Two Cases in Chinese. H. T. Hsiang.—p. 240.
Chinese Anthelmintic Prescriptions: Examples from the Han Period to the Present Time. C. S. Chao.—p. 251.

Bruxelles-Médical, Brussels

20:717-743 (April 14) 1940

- *Typhus Fever. M. Gaud and A. Pocoule.—p. 717.
Two Cases of Uteroplacental Apoplexy Treated Medicinally. R. De Guchteneere.—p. 724.
Placenta Praevia Accreta Discovered During Cesarean Section for Placenta Praevia: Subtotal Hysterectomy. R. Schockaert.—p. 729.

Typhus Fever.—Gaud and Pocoule report the epidemiologic observations made in Northern Africa on typhus fever and the successful use of a vaccine virus prepared in the Pasteur Institute of Morocco by G. Blanc and his collaborators. They attribute the endemic and epidemic recrudescences of typhus fever to the viability of the virus in the excreta of infected lice deposited on garments and thus easily transmitted, especially in times of economic distress entailing congestion and migrations. Mouse virus in fecal deposits of fleas kept dry was found to retain its virulence even after 300 days, a dose of 0.01 mg. causing infection. The vaccine recovered from fleas infected with mouse typhus and then emulsified was successful in more than 1,500,000 cases, elicited benign sequels (in only 3 per cent of the natives inoculated) and caused no deaths. Clinically the involvement of the reticulo-endothelial system is significant in typhus. Meteorologic factors may be implicated in the cyclic recurrence of the disease.

Schweizerische medizinische Wochenschrift, Basel

70:337-364 (April 20) 1940. Partial Index

- Sulfanilamidothiazole: Contribution to Chemotherapy of Coeliac Infections. M. Hartmann.—p. 337.
Id.: New Chemotherapeutics of the Sulfanilamide Series. R. Meier, O. Allemann and E. Merz.—p. 338.
Chemotherapy of Acute Infectious Diseases by Means of Sulfanilamidothiazole. O. Gsell.—p. 342.
*Comparative Clinical and Necropsy Studies of Bone Marrow. H. Jeanneret.—p. 351.
Gynecomastia with Obesity and Constitutional Acromegaly Hyper trophy, Syndrome of Hyperfunction of Anterior Pituitary. M. Schachter.—p. 357.

Necropsy Study of Bone Marrow.—Jeanneret made microscopic examinations of bone marrow in fifty-eight cases coming to necropsy. Several aspirations were made in each case by means of a sternal puncture, the first specimen being taken during the first hour after death, the others at short intervals. The cadaveric bone marrow, withdrawn less than an hour after death and examined as a stained smear, is comparable to the marrow of the living subject in cellular sharpness; it is slightly inferior in affinity to the May-Grünwald-Giemsa stain. Post-mortem alteration of the medullary elements appears in from one to three hours. It involves first the polymorphonuclear neutrophils and somewhat later the myelocytes. The nucleus of the normoblast undergoes pyknosis and fragmentation. The plasmocytes, lymphocytes and stroma cells change slowly, as do also the eosinophils. Myelocytic or erythroblastic mitosis, as well as the thrombocytes, disappears in one or two hours. The myelogram is greatly modified. The proportion of polymorphonuclears decreases rapidly, falling to zero in from eight to twenty-four hours; that of the myelocytes and of the cells of the stroma appears to increase. These processes depend only slightly on the ambient temperature, but septic conditions accelerate them greatly. Accurate study of bone marrow is possible during the three hours immediately following death; this interval is reduced by one hour and a half in the case of acute purulent infection. An anatomic diagnosis of granulocytopenia or of plasmocytoma is possible for twelve hours. It is the same with the estimation of the hemopoietic activity from the number of erythroblasts. In ten of the fifty-eight necropsies the author followed every sternal puncture by a costotomy. The medullary contents of the costal fragment were immediately pressed out and smeared on a slide. The costal marrow differs perceptibly from the sternal marrow; in the first, the proportion of stroma cells and of myelocytes as well as the quantity of fat are much greater; in the second the polymorphonuclears predominate. The author supposes that during the sternal puncture a sorting takes place among the cellular elements. The ripe cells are carried away in great numbers, whereas the less mobile young forms as well as the better fixed cells of the stroma are not. A sternal puncture may thus give an incorrect picture of the state of the hemopoietic organs. The myelogram, accord-

ing to the terminology of Arneth, will be much deviated "toward the right" and thus approach the hemogram. Sternal puncture made immediately after death will provide accurate information as to the proportion of the different elements. The author believes that necropsy is valuable in clarifying numerous unsolved problems of the bone marrow and its functions.

Chirurgia degli Organi di Movimento, Bologna

25:287-442 (April) 1940. Partial Index

Modern Trends in Treatment of Congenital Luxation of Hip Joint. O. Scaglietti.—p. 308.

*Circumscribed Cortical Osteitis. M. Paltrinieri.—p. 407.

Circumscribed Cortical Osteitis.—Paltrinieri reports nineteen cases of circumscribed cortical diaphyseal osteitis, a condition as frequent as Brodie's abscess but not well understood. It was a late complication of osteomyelitis and was caused by staphylococcus. The author found that it generally develops in childhood or during the prepuberal age. The tibia, femur and humerus are the bones most frequently involved. The most constant sign is the cyclic appearance of dull pain by night, which disappears after from two to four hours. The cortical focus shows on x-ray examination a small round zone of rarefaction, limited by thickness of the cortical portions of the diaphysis. The medullary cavity is normal. The lesion is a cavity of from 0.5 to 1 cm. in diameter, containing variable purulent material, thick pus, necrotic osseous tissue, a small sequestrum and granulation tissue. The periosteal reaction is like that of sclerosis in chronic osteitis. The disease is chronic. The treatment consists in removal of the osteitic focus followed by immobilization or of opening of the focus, draining and immobilization.

Policlinico, Rome

47:125-168 (April 15) 1940. Surgical Section

*Treatment of Acute Cholecystitis of Typhoid. F. Benedetti Valentini.—p. 125.

Intussusception of Cecal Haustra: Cases. E. Sovena.—p. 142.

Treatment of Acute Cholecystitis of Typhoid.—According to Benedetti Valentini, acute cholecystitis in the course of typhoid or during convalescence is grave and calls for early surgical intervention of cholecystostomy with drainage. The operation controls local inflammation, prevents perforation, stimulates elimination of biliary calculi (which as a rule are present in such cases) and of bile contaminated by typhoid bacilli. In acute cases it is advisable to suture the gallbladder to the parietal peritoneum under a local anesthesia and to perform a cholecystostomy with drainage three or four days later. Early cholecystostomy gives better results than cholecystectomy. The acute condition was controlled in two grave cases out of five reported by the author and a recovery was obtained. Cholecystectomy performed after perforation in three cases failed to save the patients.

Prensa Médica Argentina, Buenos Aires

27:905-956 (May 1) 1940. Partial Index

*Ascorbic Acid in Cerebrospinal Fluid. M. Castex and M. Schteingart.—p. 905.

Quinine Salts Treatment of Hearing Hallucinations. J. C. Vivaldo and A. Barrancos.—p. 938.

Ascorbic Acid in Cerebrospinal Fluid.—Castex and Schteingart made quantitative determinations of the ascorbic acid content in the cerebrospinal fluid, either normal or altered from disease of the central nervous system, of fifty-nine adults ranging in age from 16 to 70, and likewise in the cerebrospinal fluid, blood and urine of ten patients of this group. The amount of ascorbic acid averaged 0.0027 Gm. for each hundred cubic centimeters of normal cerebrospinal fluid, and 0.0021 Gm. for each hundred cubic centimeters of pathologic cerebrospinal fluid. The figures for ascorbic acid in the normal fluid were higher than those in the blood and the urine of the same patients and were independent of one another. There was no relationship between the age and the amount of ascorbic acid in the normal cerebrospinal fluid. The quantitative variations of ascorbic acid in the cerebrospinal fluid in diseases of the central nervous system were inconstant and not related to the disease or to the alterations of the fluid. Simple quantitative determination of ascorbic acid in the cerebrospinal fluid is of no diagnostic value

in determining hypovitaminosis C, as the figures may be normal in the presence of vitamin C inadequacy. The determination of ascorbic acid in the blood and urine after ingestion of vitamin C (administration of vitamin C for from eight to ten consecutive days up to a total dose of from 0.3 to 0.5 Gm. of the substance) is a reliable clinical test for the diagnosis of hypovitaminosis C.

Deutsche Zeitschrift für Nervenheilkunde, Berlin

150:97-192 (March 21) 1940. Partial Index

Craniosostenosis and Craniodysostosis. A. Mandel.—p. 105.

"Inflammatory Polyneuritis." W. Noell.—p. 119.

Pathogenesis of Foci in Multiple Sclerosis. G. Döring.—p. 146.

*Sequels After Head Injuries with Special Consideration of "Traumatogenic General Cerebral Syndrome." H. Saethre.—p. 163.

Rare Metencephalic Respiratory Disturbance: Contribution to Problem of Respiratory Movement. H. Plügge and A. J. Anthony.—p. 176.

Sequels After Head Injuries.—The material reviewed by Saethre consists of 574 patients with 589 injuries; 258 were early and 316 late cases. The importance of alcoholism is demonstrated by the fact that in 30 per cent of the new cases the patient was under the influence of alcohol when brought to the hospital and that one third of the patients with traumatic psychosis were chronic alcoholic addicts. The syndrome of commotio cerebri existed in 67.5 per cent of the head injuries. Loss of consciousness persisted in three fourths of the cases for less than two hours. Of those in which loss of consciousness persisted for more than twenty-four hours only six per cent presented the pure syndrome of commotio cerebri. Neurologic disturbances were observed in 54.7 per cent of the new cases and in 35 per cent of the late cases. In more than half of the late cases otologic symptoms predominated. Olfactory paresis and anosmia were likewise relatively frequent. Traumatic epilepsy was observed in 5 per cent. The author regards it as inadvisable to apply the term "traumatic neurosis" to the subjective symptoms of patients with head injuries; he thinks that this term should be restricted to cases in which intracranial lesions are absent. He suggests that the subjective symptoms be classified into (1) the traumatogenic cerebral general syndrome (headaches, vertigo and difficulties in thinking) and (2) psychogenic symptoms (a) primary, those due to shock and (b) secondary, the psychoreactive and compensatory symptoms. The traumatogenic cerebral general syndrome predominated in 49.4 per cent of the cases, the psychogenic symptoms in 24.8 per cent and the organic neurologic symptoms in 25.77 per cent.

Medizinische Klinik, Berlin

36:341-368 (March 29) 1940. Partial Index

Erection of Vertebral Fractures According to Böhler. J. C. Lehmann.—p. 341.

*Etiology and Early Recognition of Congenital Dislocation of Hip Joint. H. Storck.—p. 342.

*Coxa Vara, Its Cause and Treatment. P. Pitzen.—p. 344.

Technic of Plaster of Paris Cast. W. Birkenfeld.—p. 347.

Bronchial Carcinoma. J. Wätjen.—p. 349.

Trauma and Pathogenesis of Cancer. B. Ostertag and G. Mundt.—p. 351.

Influence of Blood Transfusion on Hematopoiesis in Bone Marrow. H. Wildegans and Helga Kröning.—p. 353.

Congenital Dislocation of Hip Joint.—Storck believes that deviations in the shape of the uterus, which, like twin pregnancies, are dependent on hereditary factors, establish an endogenous element, which, by deviation in the position of the fetus, elicits constrained spatial conditions causing luxation of the hip and torticollis. Since twin pregnancy is hereditarily transmitted also in the male line, the possibility cannot be denied that breech position (considered as a rudimentary twin pregnancy) and the deformities caused thereby can be transmitted by the male line. Thus dislocation of the hip could be considered as a secondary manifestation which has only an indirect connection with hereditary twin pregnancy. For the practitioner these observations suggest the necessity of careful observation of children, particularly girls, born in breech presentation. Special attention should be given to disturbances in the hip joint. Inhibition of straddling, difference in the length of the legs and asymmetries in the region of the pelvic bone may be the precursors of a dislocation of the hip joint.

Coxa Vara, Its Cause and Treatment.—According to Pitzen, congenital coxa vara develops probably on the basis of endochondral congenital disturbances in ossification. The roent-

genogram discloses a structural defect which runs from the center of the epiphysal line vertically, or slightly laterally downward through the neck of the femur, so that together with the epiphysal line it forms an upside-down Y. This defect is not really congenital, but develops later under the influence of the stress of weight. For this reason, the designation "congenital" has been rejected by some in favor of the term coxa vara "infantum." The cause of rachitic coxa vara is evident. The coxa vara of adolescence is the result of local osteomalacia of the cervical metaphysis of the femur, which in turn causes backward and downward sliding of the head of the femur. The osteomalacic process develops probably on the basis of an endocrine disorder, because it appears generally in patients with adiposogenital dystrophia or with eunuchoid gigantism. Trauma is as a rule merely an intensifying factor in coxa vara of adolescents. The treatment is determined by the cause and the nature of the coxa vara. General treatment produces results in rachitic coxa vara only. With the disappearance of rickets under antirachitic therapy the deformities of the neck of the femur disappear as a rule.

Monatsschrift für Kinderheilkunde, Berlin

82:1-132 (March 8) 1940. Partial Index

- Use of Urine of Convalescent Patients for Mitigation of Acute Infectious Diseases. M. Krebs.—p. 1.
Treatment of Nephrosis in Childhood. Ilse Schmidt.—p. 9.
Pertussis and Tuberculosis. Ickert.—p. 15.
Effect of Vitamin B₁ on Postdiphtheritic Paralysis. J. Dieckhoff.—p. 53.
"Atypical Adult Rickets Suggesting "Dysostosis Enchondralis Metaphysaria." Cured by Single Dose of Vitamin D₂: Case. E. Hassler.—p. 63.

Atypical Late Rickets.—Hassler reports the case of a prematurely born girl, now aged 6½ years, of normal mentality who had been intensively managed against rickets since her third year. When she was 4 years old, rachitic symptoms appeared in different parts of the skeletal system, especially in the distal portion of the right leg, involving talipes. Progressive deterioration caused her to be hospitalized. The laboratory tests (x-ray examination, microscopy of excised bone, blood analysis) disclosed normal processes of calcification, with extensive proliferation of connective tissue, normal phosphorus and calcium levels of the blood serum and a pathologic picture that suggested "dysostosis enchondralis metaphysaria." An inspiration prompted the author to administer a massive dose of 7.5 mg. of vitamin D₂. The child was seen again eight months later and showed a complete recovery. Skeletal modifications were scarcely noticeable in the roentgenograms.

Nervenzarzt, Berlin

13:97-144 (March) 1940. Partial Index

- Cerebral Malformations and Epilepsy. A. Bannwarth.—p. 97.
*Verification of Value of Laignel-Lavastine and Koressios' Hemolytic Serum in Treatment of Multiple Sclerosis. P. Beck and P. Martini.—p. 103.
Hereditability of Amyotrophic Lateral Sclerosis. R. Dittel.—p. 121.
Diagnostic Difficulties in Bürger's Disease of Brain: Case. V. Schretzenmayr.—p. 124.

Hemolytic Serum in Multiple Sclerosis.—Beck and Martini, instructed in the technic by Koressios, employed the hemolytic serum named after Laignel-Lavastine and Koressios in forty-six cases of multiple sclerosis and report observations strikingly at variance with the successful results recently claimed by the French originators of the serum (a rabbit serum treated with blood derived from patients with multiple sclerosis). All forty-six cases save one were either of recent origin (seven) or of somewhat less recent development (thirty-eight). Twelve had been under observation for one and a half years, nineteen for from one and a half to two years and fifteen for more than two years. Dosage, consisting initially of 0.5 cc. of the serum, had been increased, under proper control when deemed necessary. In thirty-one cases no change in the gravity or course of the disease was noted; seven showed temporary or subjective signs of improvement but ultimately had to be classed with the failures. Several of the early cases were observed to grow worse in the course of the treatment. Thirty-nine of the forty-six cases are regarded as furnishing negative results. The authors' skepticism of the favorable results obtained by the French authors is based on a more rigorous conception of what

constitutes improvement. In view of the well known variable manifestations in multiple sclerosis and the frequency of remissions, subjective ameliorations, they think, viewed against a background of unmodified objective symptoms, need to be cautiously interpreted. Even the more recent significance attached to the serum by Koressios as "group specific" for infectious diseases of the nervous system, because it evoked prolonged and extensive cutaneous reactions in multiple sclerosis and in various forms of encephalitis, is challenged by the clinical reviewers. They were able to duplicate the same reactions by means of a hemolytic rabbit serum treated with the blood of normal persons.

Zeitschrift f. d. ges. experimentelle Medizin, Berlin

107:321-466 (Feb. 19) 1940. Partial Index

- Hemothorax. H. Bauer.—p. 321.
Extrahepatic Function of Bilirubin in Exudates and Hematomas. K. Dirr and E. Klemm.—p. 338.
*Lipase Level of Blood Serum. II. Hangleiter and A. Reuter.—p. 355.
Effects of Partial Baths on Temperature of Skin. G. Riemerschmid and O. Scheurer.—p. 373.
*Has Dysfunction of Lipoid Metabolism a Specific Significance for Malignant Tumors? K. Dirr and E. Sommer.—p. 393.

Lipase Level of Blood Serum.—Hangleiter and Reuter examined 150 serums of normal controls and of patients presenting a variety of diseases by means of a modified tributyrin method in order to determine the lipase content of the blood serum. In cases of diabetes mellitus the level was generally within the lower normal limits. In cases of carcinoma and in those of liver and of gallbladder diseases the level was greatly diminished. No typical changes were observed in cases of gastritis, enteritis, pneumonia and other infectious diseases, with the exception of those of tuberculosis, in which the lipase level was low. In cases of multiple sclerosis approximately normal lipase values were found. However, the paucity of cases did not justify conclusions on the connection between lipase levels and the pathogenesis of the disease. Further tests with ingestion of food rich in fats, and with an intubation procedure conveying enzymes such as pestled pancreone in large quantities directly into the duodenum failed to augment the lipase level of the blood stream. Histamine, however, was effective in increasing lipolytic fermentation.

Dysfunction of Lipoid Metabolism in Malignant Tumors.—Dirr and Sommer examined the diagnostic validity of Ascoli's view that the serums of persons with malignant tumors possess lipoids with abundant unsaturated valences not found in normal or in other pathologic serums. By dividing the total of unsaturated valences with these labile unsaturated valences, called "disposable," Ascoli found a general quotient of 6, the relative relations between total and "disposable" valences never varying. However, in the serums of persons with malignant tumors Ascoli found a quotient of 2 to 3, attributing this change to an increase in "disposable" valences. Dirr and Sommer, testing Ascoli's method and results in a group of seventeen normal and nonlipoid labile controls, twenty-four lipid labile persons and fourteen patients with malignant tumors, were able to confirm Ascoli's view that serums of patients with malignant tumors show an increase in the number of disposable, unsaturated valences. However, they found not an absolute but only a relative increase compared with the total valence count, the total count fluctuating strongly. They, therefore, conclude that lipid metabolic dysfunction is non-specific for malignant tumors and that further investigations are needed.

Zeitschrift f. menschliche Vererbungslehre, Berlin

24:161-264 (March 12) 1940

- *Hereditary Implications in Allergic Diseases. K. G. Horneck.—p. 161.
Caries and Parodontosis in Twins. G. Nehls.—p. 235.
Relation of Constitutional Type to Class Attainments of College Seniors. G. Just and W. Kramaschke.—p. 248.

Hereditary Implications in Allergic Diseases.—Horneck investigated the history of 1,280 unselected persons, belonging to 519 families and twenty-five family groups, for a hereditary background of allergic, associated (begleitkrankheiten) and neuropathic diseases. (The term associated diseases is used to include acute rheumatic arthritis, arthritis deformans, muscular rheumatism, gout, biliary and renal calculus, ulcer ventriculi

and duodeni.) In 278 persons (21.7 per cent), of whom 116 were children, allergic manifestations either existed or had existed; associated diseases were represented in 156 and neuropathic involvements in 102. In eighty-three cases an allergy had been observed during the first decade of life, predominating among the male patients. In puberty, allergies in females gained the ascendancy and retained it until the seventeenth year (26 per cent in females against 2.9 per cent in males); thereafter allergic incipency was at a minimum. Significant allergies in female subjects consisted especially of migraine, hay fever, Quincke's edema and eczema. In adults bronchial asthma, hay fever and eczema occurred in the ratio of 10 per cent in men to 6.8 per cent in women. Unskilled labor was represented forty-eight times (20.7 per cent) in the allergic picture, skilled labor and artisans thirty-seven times (22 per cent); white collar workers such as clerks, petty officials and small tradesmen forty-nine times (22.1 per cent) and the professions twenty-three times. Allergic diseases were twice as common among urban (11.9 per cent) as among rural dwellers (4.3 per cent). Successive generations of the same family presented either the same allergy or allergic variations. Pathologic connections were directly traceable to the parents in 175 cases (62.2 per cent). Siblings of allergic persons showed no increased incidence rate in allergic and associated diseases compared with the rate of the general population, but siblings of neuropathic persons or of those with associated diseases did show an increase in allergy manifestations. Five times as many neuropathic conditions were found among allergic persons as among nonallergic—fifty-eight out of 278 (20.8 per cent) against forty-four out of 1,002 (4.4 per cent)—justifying the assumption that neuropathic conditions constitute a nutrient soil for allergic diseases. Leptosomatic and asthenic constitutional types were observed to possess a susceptibility to migraine, to acute rheumatic arthritis and to ulcer ventriculi and duodeni, whereas the pyknic and muscular type was inclined to bronchial asthma, Quincke's edema, gelosis, muscular rheumatism, arthritis deformans and biliary and renal calculus. The incidence of allergic diseases in professional family groups showed a high elevation, about 30 per cent.

Ekspperimentalna Meditsina, Kharkov

1-96 (No. 1) 1940. Partial Index

- Biochemistry of Epinephrine and Adrenogenous System. A. M. Utevskiy and V. O. Osinska.—p. 1.
Proteolysis and Aminogenesis of Hepatic and Pulmonary Tissue in Sensitization and Anaphylactic Shock. L. S. Lifshits.—p. 6.
Quantitative and Qualitative Alterations of Pancreatic Secretion: Result of Painful Irritation. S. Ya. Yaroslav and E. B. Lakezhevskiy.—p. 13.
*Methylene Blue Disinfection of Conserved Blood. E. O. Spivak and I. A. Pelishenko.—p. 21.
Determination of Water in Biologic Tests. V. G. Gurevich and L. E. Carlson.—p. 28.

Sterilization of Conserved Blood with Methylene Blue.—Spivak and Pelishenko demonstrated a definite sterilizing effect of solution of methylene blue in experiments on citrated donor's blood contaminated with *Streptococcus*, *Staphylococcus*, *Micrococcus albus*, *Bacillus coli* and *Bacillus subtilis*. Methylene blue added to the citrated blood in amounts not exceeding the therapeutic dosage, from 0.04 Gm. to 100 cc. of blood, did not alter the osmotic resistance of the red cells and did not accelerate the onset of hemolysis. Irradiation of the blood with ultraviolet rays and short waves did not enhance the disinfecting effect of methylene blue.

Sovetskiy Vrachebnyy Zhurnal, Leningrad

Feb. 29, 1940 (No. 2) Pp. 81-160. Partial Index

- Gunshot Injuries of the Chest. A. V. Smirnov.—p. 81.
Prophylaxis and Therapy of Grip. D. M. Rossiyskiy.—p. 87.
Gonorrheal Arthritis. I. M. Porudominskiy.—p. 95.
*Evaluation of Therapy of Pulmonary Suppuration. I. V. Neymark.—p. 101.
Repercussive Anisocoria in Peripheral Nervous Lesions. N. E. Osokin and E. M. Dovgiallo.—p. 109.
*Hypertonic Solution of Sodium Chloride Therapy of Trichomonal Vaginitis. Y. L. Dozortseva and R. S. Lifshits.—p. 121.

Pulmonary Suppuration.—So far as treatment is concerned, there is no need, according to Neymark, to differentiate between gangrene and abscess of the lung. The belief that gangrene of the lung is caused by anaerobic micro-organisms while the

abscess is caused by aerobic ones has been disproved. The microflora may be identical in the two conditions, since both are apparently stages of the suppurative process. The post-operative mortality rate of the various surgical clinics is rather high (32 and 58 per cent). Most surgeons advise waiting from six weeks to two months after the onset of the symptoms before resorting to surgical intervention. Evaluation of conservative methods based on an analysis of the author's seventy-four cases is as follows: 1. Arsphenamine may be tried in the presence of fusiform spirochetal infection. It is contraindicated in suppurations on a tuberculous basis because of the tendency to provoke hemoptysis and febrile reaction. 2. Roentgen therapy is contraindicated in chronic abscess associated with bronchiectasis. It provokes in these cases spitting of blood and sharp rises of temperature. 3. Intravenous administration of 20 per cent alcohol proved to have an undoubted favorable effect on the acute abscess. It does not provoke hemoptysis or raise the temperature. It is not effective in chronic suppuration. 4. Oral administration of capsules containing potassium permanganate had a favorable though transient effect on chronic abscess. 5. The best results were obtained from the combination of the alcohol and the permanganate therapy. This effect is probably due to the oxidizing of the pulmonary tissue, rendering the soil less favorable for the bacterial flora and to its direct though mild bactericidal effect.

Trichomonal Vaginitis.—Dozortseva and Lifshits treated 100 patients with trichomonal vaginitis with hypertonic solution of sodium chloride. The majority of the patients were aged from 21 to 35. Practically all presented on examination a granular colpitis with hyperemic mucosa, irritation of the external genitalia and local tenderness on vaginal examination. In about 50 per cent there was associated gynecologic disease. Smears revealed numerous cocci and many leukocytes. The pH of the vaginal secretions in many of the cases was from 6 to 7. Apparently *Trichomonas* can live and multiply in weakly acid, neutral and alkaline mediums. The treatment consisted of a daily vaginal douche with 1 liter of a 25 per cent solution of sodium chloride (one glass of kitchen salt to a liter of water) at a temperature of 38 C. Discharge was controlled, as a rule, after five or six treatments, and the *Trichomonas* were no longer present after from ten to fifteen douches. Colpitis and vulvitis disappeared simultaneously. The pH of the vaginal secretions rose in many instances to 5. While the method is effective, it does not guarantee against recurrence. The authors advise that the douches be continued for some time after the *Trichomonas* have disappeared from the discharges.

Vrachebnoe Delo, Kharkov

22:1-80 (No. 1) 1940. Partial Index

- New Paths in Treatment and Prophylaxis of Myopic Chorioretinitis. V. P. Filatov.—p. 1.
Blood Sugar and Chloride Levels as Index of Physiologic Status. G. V. Folbert.—p. 5.
Symptomatology and Pathogenesis of Extracapillary Nephritis. F. I. Litvak and D. D. Zaydenberg.—p. 11.
Pathologic Alterations in Hypophysis in Renal Disease. B. P. Kucherenko.—p. 31.
Roentgen Diagnosis of Malignant Tumors of the Kidney. M. M. Vaysfilgel.—p. 37.
*Ultraviolet Irradiation in Grip. S. E. Vitebskiy.—p. 47.

Ultraviolet Irradiation in Grip.—Vitebskiy reports the effects of ultraviolet irradiation in 625 cases of grip observed during the epidemic of 1935-1936. The treatment was begun on the first day of sickness in 308 cases, on the second in 170, on the third in 112 and on the fourth in thirty-five. It consisted of a daily suberythemic dose of ultraviolet rays to the anterior and the posterior surfaces of the thorax. The minimal number of exposures was three and the maximal six. The temperature fell to normal after the first exposure in 55 per cent of the first group, after two exposures in 33 per cent and after three exposures in 12 per cent. In cases in which the treatment was begun on the second day of illness, the temperature came down to normal after one exposure in 51 per cent, after two exposures in 30 per cent and after three exposures in 19 per cent. In cases in which the treatment was begun on the third and the fourth day, the temperature came down to normal after the first exposure in 17 per cent, after the second in 30 per

cent and after the third and fourth in 53 per cent. It is thus apparent that the earlier the treatment was begun the quicker was the return of the temperature to normal. Along with the lowering of the temperature there was noted improvement in the subjective and the objective symptoms. The number of sick days in instances in which the treatment was begun on the first or second day amounted to three, which is from one and a half to two times less than in cases in which irradiation was not given. A favorable effect was likewise noted on diffuse postgripal bronchitis in a group of forty cases in which the treatment was begun on the third or the fourth day. The treatment here was extended to from six to ten exposures. There was not a single instance of bronchopneumonia or any other complication.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

80:917-988 (April 9) 1940

Secondary Glaucoma in Presence of Anterior Synechia. A. W. M. Houwer.—p. 918.

Tattooing of Corneal Leukomas with Candle Soot. A. W. M. Houwer.—p. 927.

*Xerophthalmia Among Children in Batavia. J. H. de Haas, J. H. Posthuma and O. Meulemans.—p. 928.

Operations for Cataract and Treatment of Xerophthalmia in the Netherlands East Indies. J. Tijssen.—p. 951.

Xerophthalmia Among Children in Batavia.—According to de Haas and his collaborators, 259, or nearly 5 per cent, of the children admitted to the Central Civil Hospital in Batavia during the period from 1935 to 1938 had xerophthalmia. More than 40 per cent of these children were either totally blind or blind in one eye. Disorders of the digestive tract occupied a prominent place among the diseases coincident with xerophthalmia, and it is probable that inadequate resorption and insufficient diet play an important part in the pathogenesis of xerophthalmia. Feeding with sweetened skimmed milk was responsible for two thirds of the total number of cases of xerophthalmia in children less than 2 years old. An advanced state of dystrophy existed in 75 per cent of the children with xerophthalmia. The vitamin A content of the blood was lower in children with xerophthalmia than in those without it. Vitamin A and the continued oral administration of cod liver oil is recommended for the treatment of xerophthalmia, particularly during the early stages. Prophylaxis is more important than treatment; it should be directed toward improvement of the nutrition of the natives, particularly of children of the preschool age.

Acta Radiologica, Stockholm

21:119-230 (April 30) 1940. Partial Index

Half-Axial Projection in Accentuated Lordosis for Roentgen Studies of the Lungs. K. Lindblom.—p. 119.

Bone Defects in Terminal Phalanges. N. Frostberg.—p. 126.

Polycystic Fibrous Dysplasia. T. Denstad.—p. 143.

Diagnosis and Roentgen Treatment of Certain Forms of Lumbago. C. I. Bastrup.—p. 151.

Myeloscopic and Myelographic Aspects of Posterior Protrusions of Intervertebral Disk Causing Sciatica. W. G. Deucher.—p. 164.

*Comparison Between Roentgenologic and Operative Findings in Acute, Mechanical Ileus. S. A. Chrom.—p. 182.

Studies on Liberation of Sulfuric Acids from Granules of Mast Cells in Subcutaneous Connective Tissue After Exposure to Roentgen and Gamma Rays. B. Sylvén.—p. 206.

Roentgenologic and Surgical Aspects in Ileus.—Chrom evaluates the diagnostic value of roentgenoscopy in cases of acute mechanical ileus on the basis of thirty-two patients admitted to the State Hospital in Copenhagen during the years 1935 to 1938 inclusive. In nineteen of the cases the x-ray examination was made within one hour before the abdomen was opened. In sixteen of these the condition seen on operation agreed with those seen in the x-ray examination, the latter having shown distention of the small intestine alone in eight cases, of the colon alone in five and of both the small intestine and the colon in three. In the remaining three cases the surgical and x-ray observations did not agree. The author concludes that it is generally possible to obtain information regarding the localization of bowel distention by means of x-ray examination of the abdomen without the use of a contrast medium. Fluid levels were present in the roentgenograms in the majority of the cases of surgically verified ileus of the small intestine and in

all cases of ileus of the large intestine. Roentgenograms of the abdomen made without a contrast medium do not, however, furnish precise information about the cause, nature and localization of ileus of the small intestine. In these cases judgment must be based chiefly on the history and clinical manifestations, for although the administration of contrast medium by mouth may provide more exact information it will be contraindicated or impossible to carry out in the majority of cases. The situation is quite different in cases of ileus of the large intestine, because here a contrast enema makes it possible to localize the site of obstruction. The author was able to prove this in all twelve cases of mechanical ileus of the colon. A contrast enema was given to nine patients with ileus of the small intestine and the impression was gained that the subsequent roentgenoscopy constitutes a valuable diagnostic aid because it may determine that the obstruction is not in the colon, but it may localize the obstruction and in many cases determine its nature.

Ugeskrift for Læger, Copenhagen

102:255-286 (March 21) 1940

*Frequency of Disk Prolapse as Cause of Sciatica. T. Andersen.—p. 255.

Apparatus for Oxygen Treatment in Cases of Lung Gas Poisoning. O. Bang.—p. 268.

Emergency Mask for Oxygen Treatment in Cases of Phosgene Poisoning. A. Eldahl and M. Vermehren.—p. 274.

Prolapse of a Disk as a Cause of Sciatica.—Andersen made myelographic examinations in eight cases of severe sciatic neuritis in which other methods of examination (gynecologic examination, rectal exploration, roentgen examination of the vertebral column and pelvis) had failed to explain the symptoms. In all the cases myelography showed defects in the contrast shadow which agreed with the symptoms. Operation, done in three of the cases, revealed the prolapse of two disks in one, prolapse of a disk with thickened ligamentum flavum in one and both prolapse of a disk and thickened ligamentum flavum in one. The observations at operation corresponded closely with the results of myelography. The remaining five cases were believed to present similar disorders. Attention is called to the similarity between the classic picture of sciatica and the typical picture of prolapse of an intravertebral disk or thickened ligamentum flavum in the lower lumbar column. The author concludes that apparently idiopathic sciatic "neuritis" probably most often depends on intraspinal disorders, first of all prolapse of a disk or thickening of ligamentum flavum. He advises myelography only on patients so disabled that operative treatment is to be recommended if the results of myelography testify to an intraspinal lesion. In the great majority of cases treatment should be conservative, he says. These lesions of the vertebral column do not always cause sciatica. The symptoms depend on where in the spinal canal the prolapse of the disk or ligament thickening is located.

102:349-384 (April 11) 1940

*Lines of Guidance in Roentgen Therapy of Leukoses. C. Krebs and J. Bichel.—p. 349.

Methylene Blue as Means Against Methemoglobinemia During Treatment with Chemotherapeutics of Sulfanilamide Group. J. L. Hansen.—p. 352.

Lines of Guidance in Roentgen Therapy of Leukoses.—Krebs and Bichel state that the best treatment for myeloid and lymphatic chronic leukoses is irradiation which can be supplemented by other means, especially treatment with arsenic. Therapy must be individualized. The aim should be as good a general condition as possible without regard to changes in the leukocyte values. The authors emphasize especially that the absolute leukocyte count plays a subordinate role in relation to the qualitative composition of the white blood picture. Roentgen therapy should be interrupted when subjective improvement has set in, even if the leukocyte count is still high. Relative increase in the number of immature forms in the blood picture contraindicates continued therapy. Complete blood examinations twice a week, and frequently more often, are necessary during treatment. The tolerance to roentgen therapy varies greatly, consequently treatment should in all cases begin with small doses.

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THE BLOOD BANK OF THE JOHNS HOPKINS HOSPITAL

MARK M. RAVITCH, M.D.

BALTIMORE

For many years the pediatric service of the Johns Hopkins Hospital has stored citrated blood in 500 cc. quantities as drawn from adult donors, to be parceled out to one or several recipients. This practice arose from the necessity for small transfusions and from the inconvenience of taking repeated small amounts from donors. The surgical service has also drawn blood in anticipation of its use for one patient and occasionally has found it convenient to give it to another. This blood was stored for varying periods, on one occasion as long as seventeen days. These small and occasional blood stores constituted informal banks and differed essentially from the routine practice in transfusions at the time only in that the blood was kept in the transfusion system (or at times poured over into sterile flasks) for days instead of minutes between being drawn and administered. In the early part of 1939 the work of the Cook County Hospital in Chicago led to the establishment here of a blood bank suited to our purposes, and the bank was opened in March.¹ After a period of several months a combination of circumstances, some to be detailed later, led to the necessity for the adoption of new rules and for a reorganization. The difficulties which arose and the measures taken to obviate them are of some interest. The horizontal disposition of the hospital units (built on the old "pavilion" plan instead of the modern, vertical, skyscraper plan) presented physical difficulties, and the strict division of personnel into the several hospital services complicated the problem of organization. The considerable proportion of Negro patients also constituted one of the primary problems. Although there is, of course, no valid objection on biologic or physiologic grounds to the transfusion of patients of one race with blood from donors of another, it has been deemed best to avoid the issue.

At present the services participating in the blood bank are the surgical, medical, obstetric, gynecologic, urologic, orthopedic and otolaryngologic. The pediatric service has not joined the blood bank because the children's unit is not sufficiently convenient to the building in which the bank is located. A technician is on duty in the bank between the hours of 9 a. m. and 5 p. m. six days a week. He performs the groupings and cross matchings, keeps the records and sees that the blood stores are maintained. The care of the appa-

ratus, its maintenance, washing and wrapping for sterilization are also the responsibility of the technician. He is supervised by the physician in charge of the blood bank, at present one of the assistant resident surgeons, who carries this in addition to his other duties. It has been found that a major requirement for successful functioning of the bank is centralization of authority and responsibility. To further this end, one house officer from each member service is made responsible to the bank for all blood transfusions done in his service. This house officer is responsible for everything connected with transfusions in his service—drawing blood, giving blood and grouping and matching bloods when the technician is not available. In addition, one assistant resident in each service has been designated to supervise the work of his house officer.

The bank is housed in a small room adjoining the laboratories of the Biological Division of the Medical Clinic. The room is furnished with the technician's desk and microscope, a table for centrifuge and shaking machine, a long table for wrapping the transfusion sets, and a two burner gas range for boiling and processing tubing and glassware. There is also a large sink equipped with several spigots to which tubing may be directly attached. The sink is lined with sheet sponge rubber to minimize breakage of glassware. A drainage rack for bottles and a cabinet for supplies and the storage of sets complete the equipment. The transfusion sets are sterilized in the autoclaves of the central sterile supply room of the hospital. The blood is stored in one compartment of the refrigerator of the Biological Division, in which the temperature is kept constantly at 35 F. The compartment contains two shelves, one for blood from white donors and one for blood from Negro donors.

In establishing an initial supply of blood for the bank it was necessary to use as donors members of the family of any patient who was ill enough so that the announcement of the possible need for transfusion would not be an added cause for alarm. In some instances two donors were bled when a patient needed a transfusion, the second flask of blood going into the bank. In addition, the obstetric service found it easy to obtain blood from the families of women taken to the delivery floor, since the possibility of severe hemorrhage during childbirth is recognized by the public. The same sources are used to make up bank deficits which result when blood is out of date, when a recipient has neither family nor friends to serve as donors or when a recipient dies before the blood which he has used can be replaced. Blood obtained from the bank for private patients must be repaid with blood and may not be bought directly from the bank for cash. The blood for replacement must be obtained either from a family donor or from a professional donor paid by the patient.

From the Department of Surgery and the Biological Division of the Department of Medicine of the Johns Hopkins University.
1. Most of the original work and experimentation with apparatus, technique and organization was done by Dr. Russell Williams, then resident physician.

We have also occasionally used convalescent patients as donors. Therapeutic venesections are an infrequent source of supply.

In a hospital the size of ours,² and with the volume of transfusion done (from 100 to 110 transfusions monthly through the bank), and particularly in view

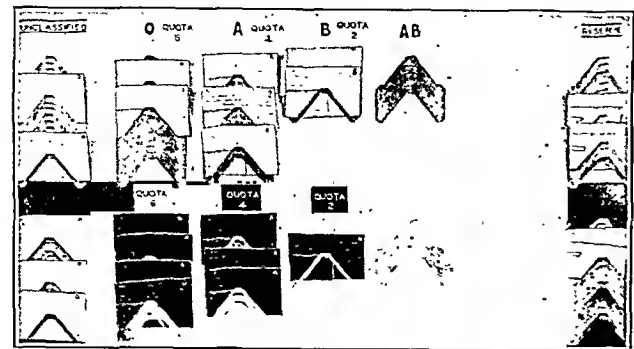


Fig. 1.—The bank board. There is a card on the board for each bottle of blood on hand. The blood that is "on reserve" is included in the quota. Cards for blood from white and from Negro donors are filed in the appropriate halves of the board.

of the fact that we were running two entirely separate small banks, for white and for Negro patients instead of one larger one, it was found necessary in the trial period to maintain a close watch over the flow of blood into and out of the bank. If blood was drawn for the bank without regard to the group, excesses in the rare groups occurred which, in the period of storage, were not corrected by a corresponding demand. It was further found that to permit services to "build up a credit" when more blood was available than they owed was to permit the accumulation of more blood than could be used before the expiration date. For this reason we have established a quota system. The original quota was, for each race, five flasks of O blood, four flasks of A blood, three flasks of B blood and no flasks of AB blood. We have since revised these quotas to five, four and two for the white and six, four and two for the Negro race (fig. 1). When donors present themselves, the house officer in the ward questions

FORM 3073 THE JOHN HOPKINS HOSPITAL

REQUEST FOR BLOOD GROUPING & MATCHING

NAME _____ A.M. _____ P.M. _____ Hist. No. _____

Date _____ Hour _____

Diagnosis _____

Blood group _____ Signed _____

Bank ☐ CHECK ☐ Emergency

Professional ☐ ONE ☐ To be transfused as soon as matched

Family ☐ ☐ To be transfused but not urgent

☐ Precautionary matching

☐ Group and Hold

☐ For operation on (date) _____

Fig. 2.—Type of slip used for request for blood grouping and matching.

them with regard to syphilis and antisyphilitic treatment and performs macroscopic groupings, equipment for which purpose, supplied with high titer grouping serums, is present in every ward. The bank is then offered its choice of blood in the available groups. Our quota restrictions are not rigid and we permit an excess of one or even two flasks in the O or A group. In group B we discourage an excess because of the slow

turnover. An attempt is made to keep the total number of flasks of blood on hand constantly at or near the maximum.

It is optional with the house officers whether the serologic test for syphilis is performed before or after the blood is drawn. Serologically positive blood is discarded, of course, but the time wasted in drawing such blood is compensated for by the saving of time to interns and donors in drawing blood without delay. An economy resulting from the institution of the bank has been the elimination of the expense of having technicians or call for emergency serologic determinations on donors. If emergency transfusions at night are needed in the pediatric service or in the private wards, and professional donors are not wanted, bank blood is supplied.

During the trial period all donors were required to have negative serologic tests for syphilis before blood could be drawn. At the same time house officers had not yet become accustomed to giving blood to their patients before drawing blood from a donor. It frequently resulted that, while waiting for the serologic report and before drawing blood from a donor, the house officer would match the donor's blood against that of the patient. When these happened to be of the same group and were compatible, the house officer often decided to use the donor on hand instead of taking "old

FORM 3075 THE JOHN HOPKINS HOSPITAL

REPORT OF BLOOD GROUPING & MATCHING

AM _____ Hist No. _____

Date _____ Hr. _____ PM Requested by _____

The blood of _____

NAME _____ COLOR _____ WARD _____ SERVICE _____

Blood group _____ is matched and is compatible with,

Bank blood No. _____

Professional donor _____ Group _____

Family donor _____

Matching checked by _____ Signed _____

Checked on ward for correspondence of:—Name of patient; No. on card; No. on this slip; No. on bottle.

Signed _____

HOUSE OFFICER OTHER THAN ONE TRANSFUSING.

Fig. 3.—Type of slip used for report of blood grouping and matching.

blood" from the bank for his patient and repaying the bank with fresh blood from the donor. The obvious consequence was that the turnover of bank blood was slow and small, a high proportion of bloods remained unused over the original seven day limit and difficulty was encountered in replacing the blood. It was therefore required that all transfusions on ward patients of the member services be done through the bank. In the private services the use of the bank is optional. In specified conditions, when approved by the resident or head of the service, exceptions to the use of bank blood are made. Leukemia, granulocytopenia and purpura have been the chief diseases for which the use of freshly drawn blood is indicated. For severely jaundiced patients we prefer to use the freshest blood in the bank rather than to follow the usual practice of using the oldest blood first.

In the trial period of the bank, from March through July, blood was kept for only seven days. We have increased the period of maximum permissible storage to ten days, but for the past six months the average age of blood when used has ranged from month to month between three and one-half and four and one-half days.

BOOKKEEPING

An effort has been made to reduce to a minimum the "paper work" of the bank. The specimens of a

2. In the member services there are a total of 408 public ward beds.

prospective recipient's cells and serum are sent to the bank with the request slip (fig. 2), which indicates the degree of need for the blood. After the matching has been completed this slip, with the number of the compatible blood noted on it, is filed alphabetically in its service file, to be removed at the end of the month and stored. The same information is kept permanently available for ready reference in a ledger arranged chronologically. The report slip (fig. 3), with gummed back for easier pasting in the history, is clipped to the transfusion card, the two are placed in the reserve file on the board (fig. 1), and the house officer who made the request is notified. Each morning inquiry is made of the house officers who signed the requests of the previous day as to the need for prolonging the reservations. Because patients can now be grouped, matched and given transfusions in less time than it formerly took to call in and bleed the already matched family donor, it is hardly necessary to match bloods in advance except before operation or delivery, or in the presence of hemorrhage or continuing shock.

Each service has a small book ruled as in figure 4. In depositing blood in the bank the house officer writes in the book the number of the blood and checks the

SURGERY																							
BLOOD PUT IN BANK								BLOOD DRAWN FROM BANK								BLOOD OUT OF DATE OR SPOILED							
DATE	#	COLOR	GROUP					#	COLOR	GROUP						#	COLOR	GROUP					
		W	C	AR	A	B	O		W	C	AR	A	B	O			W	C	AR	A	B	O	
12-1-39	511	✓						507	✓							488	✓						OUT OF DATE
	512	✓						495	✓														
	513	✓						493	✓														
12-2-39	515	✓																					
12-3-39								518	✓														
								519	✓														
12-4-39	527	✓														527	✓						OUT OF DATE
12-5-39	530	✓																					
12-6-39								514	✓														
								510	✓														
12-7-39	539	✓						530	✓														
	540	✓																					
	541	✓																					

Fig. 4.—Record of blood on hand in the blood bank as it appears in "small book."

race column, and after the technician has microscopically confirmed the macroscopic grouping of the blood, the group column is checked. When withdrawing blood the house officer enters the number of the blood and checks the appropriate column for group and race. The third division is kept by the technician. The house officers accredited to the bank are informed each morning of the debts of their respective services, which they are expected to make good in twenty-four hours. Bloods unused at the expiration of ten days, or found to give a positive or doubtful serologic test for syphilis, are withdrawn from the bank and charged against the service which drew them. Twice a week forms are sent out to all assistant residents reading as follows: "The blood bank has on hand the following bloods, ColoredO,A,B,AB, WhiteO,A,B,AB [the number of each is indicated] which will be out of date on [day and date of next notification day]. We should be glad to have this blood used."

The blood transfusion cards are taken to the wards, together with the matching reports, at the time of transfusion. The report slip must be initialed at the

bedside by a house officer other than the one giving the transfusion, in evidence that card, report and bottle tag correspond as to group, number and name of recipient. The cards remain in the ward, and in the appropriate spaces the nurse fills in the recipient's name, age, race, history number, the pretransfusion



Fig. 5.—Donor set. This is all that is taken to the ward for drawing blood: the wrapped donor set, the bottle, containing 50 cc. of 5 per cent sodium citrate, sealed with a metal cap and protected by a hood, the numbered transfusion card and tag, and the muslin sack for the small tubes with the donor's cell suspension and serum.

temperature and the temperature one, two, three and four hours after transfusion, together with a definite statement as to the presence or absence of a chill, urticaria or other form of reaction. When these cards

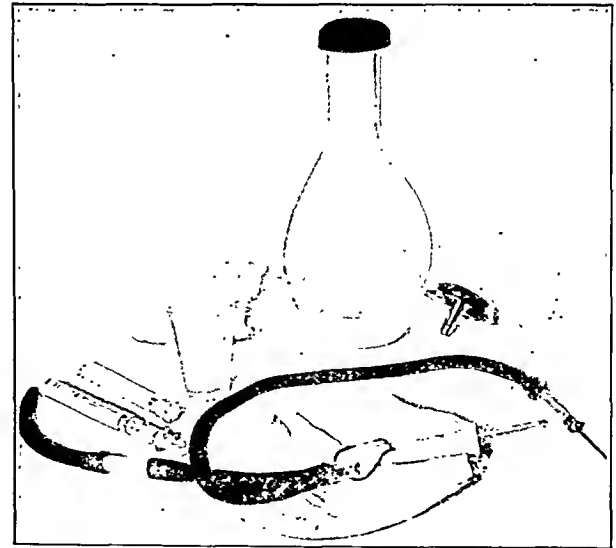


Fig. 6.—Donor set unpacked, cap removed from bottle, ready for insertion of the vent tube. Note that the two arms of the tube pass through the two holes in the cloth shield, which is packed with the outer side uppermost, minimizing the possibility of contamination during insertion. After insertion the rubber band is slipped down around the neck of the bottle. The small wrapped package contains a sterile metal cap with which to seal the bottle when the blood has been drawn. The syringe for procaine hydrochloride is packed in the Wassermann tube for protection against breakage.

are returned to the bank they are checked by the assistant resident in charge. All admitted and suspected reactions are investigated.³

3. It is planned to discuss the statistics of the bank's work and an analysis of transfusion reactions when a larger number of transfusions shall have been given than the 600 or more in the first six months since reorganization.

DRAWING BLOOD

The house officer takes to the ward the donor set (fig. 5), a blood bottle in which there is already 50 cc. of 5 per cent sodium citrate for the 500 cc. of blood usually drawn, a numbered transfusion card to which is attached a tag with the same serial number and a small cloth sack. A brief history is taken from the

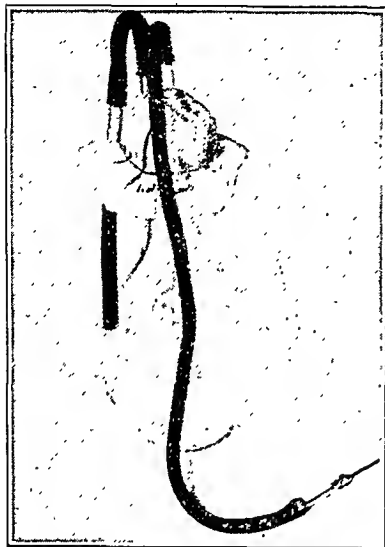


Fig. 7.—Bottle with donor vent tube in place, rubber bushing kept sterile by cloth shield. The gauze plug visible in the glass connecting-tube is an air filter in the suction line.

donor, the skin, pharynx, heart and external genitalia (of males) are examined, the blood pressure is taken and the appropriate data are entered on the transfusion card in the spaces provided. The antecubital fossa is cleaned with iodine and alcohol, a tourniquet is applied, and with procaine hydrochloride a tiny bleb is raised in the skin over the vein. The procaine syringe and needle are in the donor set (fig. 6) and the procaine is provided in the ward. Eventually a

central bleeding

room may be established adjacent to the bank, but at present the bleeding is done in the treatment room in the ward of the ostensible recipient for whom the debt was incurred. It is not necessary for the operator to wash, to scrub or to wear sterile gloves. It is far safer for him to remember that his hands are not sterile and to observe the elementary precaution of avoiding contact with the needle, the prepared skin or the por-

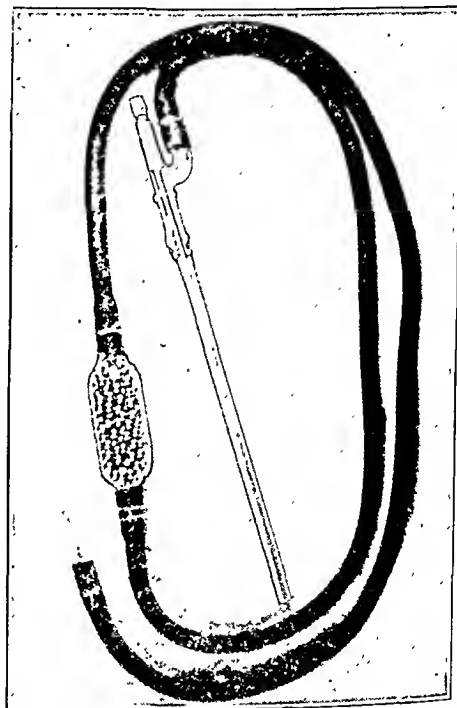


Fig. 9.—Recipient set unpacked. The stainless steel ball bearings are contained in a filter chamber incorporated in the tubing line. The vent tube is longer than that used in drawing blood (figs. 12 and 13).



Fig. 8.—Recipient set, bottle of blood, transfusion card, and cross matching report. This is all that is taken to the ward for administering blood. The small cloth bag and contained tubes are left behind in the bank.

tion of the vent tube which enters the bottle. The bottle is inverted once so that citrate will moisten the metal plunger, which in turn, as the metal cap is withdrawn, moistens the sides of the hole in the rubber bushing for easier subsequent insertion of the vent tube. The metal cap is removed from the bottle with the cloth cover in place so that the cap may be freely

handled without fear of contaminating the rubber bushing, cap and cover being removed together. The vent tube is held between the fingers at its junction with the rubber tubing, the muslin shield protecting the portion which must remain sterile. The vent tube is inserted through the rubber bushing and the shield held in place by the rubber band as shown in figure 7. Pumps are available for application of negative pressure, but our house officers usually prefer to use oral suction and are permitted to do so. A 16 gage needle is used. While the blood is being drawn, the flask is tilted so that its rotation will produce an accentric motion of the blood. When 500 cc. of blood has been drawn the tourniquet is released and a hemostat clamped across the tubing at its connection with the vent tube. If there has been any clotting in the process of drawing the blood it has taken place in the rubber tubing, and the clamp prevents the clots from entering the bottle. The needle is withdrawn, the vent tube removed from

the bottle and the bottle capped with the separately wrapped metal cap included in the set (the small wrapped object in figure 6). The clamp is now released and the blood in the tubing permitted to flow into three tubes, all contained in the set. On one there is already pasted a request slip for the STS (serologic test for syphilis) across which is stamped a red stripe. The stripe permits the Wassermann laboratory technicians to separate the blood bank STS reports from the 400 daily other reports, thus avoiding much delay. Whole blood is added to the second tube for serum, and in the third two drops of blood are added to 8 cc. of 0.85 per cent saline solution, a small flask of which is found on every ward venipuncture tray. The last two tubes are labeled with adhesive tape and placed in the cloth bag, which is hung from the neck of the bottle. The number tag is also hung from the bottle, and on this tag the technician later adds the donor's group. The STS tube is sent to the Wassermann laboratory. The

transfusion card is placed in the unclassified rack on the bank board (fig. 1), the bottle of blood is put in the refrigerator and an entry is made in the service book.

Since the pictures of the apparatus were taken we have made several changes. The citrate is added to the empty blood bottle before sterilization, and there is therefore no need for the medicine glass. The donor set is now a much smaller package and, like the recipient set, is compactly wrapped in a cardboard box cut down from a box for rubber gloves. For a time two small test tubes were included in the donor set, one for the STS, the other containing a weighed amount of sodium oxalate so that from a single tube of oxalated blood the bank technician derived both cells and serum. This plan did not prove to be worth the additional work entailed.

GROUPING AND MATCHING BLOOD

The cells are grouped microscopically by the petrolatum sealed hanging drop method. High titer grouping serums are used, and in ordinary practice groupings may be read at once, although occasionally a group B or an AB will be found to agglutinate very slowly, so that we make a practice of checking the grouping after twenty minutes. When the grouping has been checked and the STS report received and pasted on the transfusion card, the card is placed in the proper group column.

When blood is needed for a transfusion there are sent to the bank two tubes, one containing the patient's clotted blood, the other two drops of his blood suspended in 8 cc. of 0.85 per cent saline solution. We require each tube to be labeled with adhesive tape. The request slip accompanies the samples. The patient's blood group is determined and his blood cross matched with the oldest available blood of the same group and race. If the same group is not available, or a good matching is difficult to achieve, we use group O blood. Matchings are agitated for fifteen minutes and permitted to stand fifteen minutes longer before being read. In acute emergencies we feel justified in shortening these periods. Although we demand that a matching show no agglutination or hemolysis on either the "major" or "minor" side when donor and recipient are of the same group, we disregard the minor (donor's serum-recipient's cells) side when using group O blood for recipients of groups A, B or AB, since almost invariably there is immediate agglutination. All matchings, whether done by the technician or at night by a house officer, must be approved either by an assistant resident or by the bacteriologist in charge of the laboratory of the Biological Division.

GIVING BLOOD

The house officer takes to the ward (fig. 8) the recipient set, the bottle of blood, the transfusion card and the attached matching report after making an entry in the service book. The small tubes with cells and serum are left behind for recheck in the event of a reaction. We have followed the lead of other blood banks and administer our blood unwarmed except for exposure to room temperature during preparation for



Fig. 10.—Filter chamber, showing funneled inlet, two hole outlet in glass tube projecting from the bottom.

the transfusion. It may be noted parenthetically that in the surgical service we have for almost a year given fluids at room or at icebox temperature, with no discernible ill effects. Occasionally, however, cold blood or intravenous fluids will cool the skin over the receiving vein below the point of comfort. Numbers, names and groups having been checked as required, the bottle is inverted several times and the metal cap is removed. Because the blood is drawn warm, hermetically sealed, and then placed in a refrigerator, there is formed a partial vacuum and the inrush of air during removal of the metal cap is audible. The long vent tube is now inserted, the bottle inverted and air driven from the system. It is necessary to hold the inverted bottle down and the tubing up, these positions being slowly reversed in order that the bead filter chamber may fill slowly and not trap air (figs. 9, 10 and 11). If the vein is not large, house officers are advised to use a syringe and needle for the venipuncture, to twist off the syringe and replace it with the glass adapter of the transfusion set. We have discarded the old metal three way stopcocks as unsatisfactory because they leaked, were expensive and were almost impossible to clean. A transfusion of 500 cc. is expected to take at least half an hour. By stripping the tubing this quantity of blood may be forced into the vein of a patient in collapse in ten minutes. House officers are responsible for the prompt return of all apparatus to the bank.

Blood which passes the expiration date or which is found to be serologically unsuited is not wasted. It is used in various laboratories for culture mediums and for experimental work in which human blood or plasma is required. Our own experiments with various filters have utilized a considerable quantity of this blood. In addition, it must be recalled that an "unused" blood may have been matched several times against patients in the operating or delivery rooms and so served a protective function for those patients, although it never found its way into their veins. We now separate the plasma from out of date blood to be used in cases of shock without hemorrhage, as well as in hypoproteinemia. A previous step in this direction was the use of plasma from currently usable bank blood for such cases, and its replacement in the bottle with 5 per cent dextrose, the resultant suspension of red blood cells in 5 per cent dextrose being designated for transfusions in patients in whom anemia is the principal indication.

THE APPARATUS

The vent tubes used for taking and giving blood are identical except for their lengths. The portion of the tube which passes through the rubber bushing contains an inner channel through which there is a flow continuous with that in either end of the straight tube. This channel is surrounded by a jacket which has two small inflow orifices inside the bottle and connects with the right angled tube externally. For drawing blood



Fig. 11.—System filled with blood, ready for insertion of needle. The end of the vent tube projects above the level of the blood (fig. 13).

(fig. 12) a short tube is used so that the flow of blood from the tube end may be observed. The rubber tubing containing the gauze filter unit, through which suction is exerted, is put on the angled side arm and the blood flows through the straight tube, while the holes in the

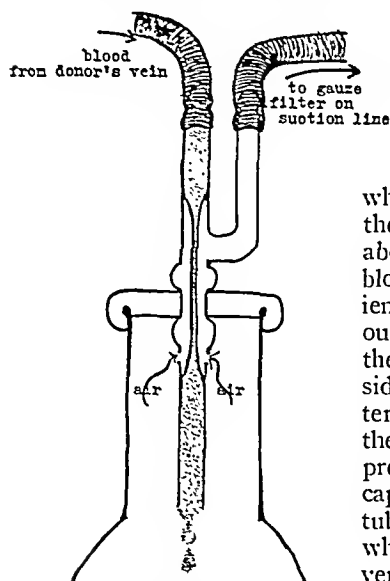


Fig. 12.—Detail of vent tube as used in drawing blood. Blood flows through central channel. Air is evacuated from flask through the vent holes connecting the jacket with the side arm. Short tube permits observation of the rate of flow of the blood.

tory for the administration of blood, although quite satisfactory for the administration of other fluids.

THE FILTER

The realization that in all stored blood there is invariably found, within a few hours, a considerable quantity of fibrin shreds and clots, regardless of the freedom from clots of the blood when first drawn, led us to consider the use of filters. We have assumed, to begin with, that these shreds and clots are undesirable and perhaps harmful, although, aside from the obvious possibility of mechanical interference with the smoothness of the transfusion, that point has yet to be proved. Some idea of the quantity of clot to be found may be had from figure 14. The total in the three glass dishes was contained in one 500 cc. sample of blood just twelve days old. The filter recommended for our flasks by the manufacturers requires removal of the rubber bushing, which we were anxious to avoid. We have tried the commercial stainless steel mesh filter. It is very efficacious but so constructed that whenever there is much clot the flow of blood is reduced to a trickle. The use of beads was suggested by Boland and his co-workers,⁴ who described a method of blood transfusion proposed for the British army. They placed glass beads in the vessel into which the blood was to be drawn. We have objected to this arrangement on the ground that introduction of the beads at this point, with the subsequent unavoidable shaking of the bottle, produces hemolysis as well as a tendency to defibrinate the blood. At first we introduced the beads into the bottle at the time of administration of the blood. The beads were contained in a 2 foot length of stiff rubber tubing, with an inside diameter less than twice the diameter of the beads. The tube was filled with beads and the two ends

jacket permit the evacuation of air from the flask. In administering transfusions (fig. 13) very long tubes

are used so that when the flask is inverted the tube end projects above the level of the blood. In these recipient sets the blood flows out of the bottle through the jacket and out the side arm, while air enters the flask through the straight tube. If the precaution is taken of capping the projecting tube end with a finger while inserting it and inverting the bottle, blood will be prevented from dripping down the air intake tube. We have found the capillary vent tubes supplied by the makers of this apparatus unsatisfactory

were joined by a coupling of slightly larger stiff tubing. The tubing was uncoupled, care being taken to keep the ends sterile, the small end was fitted to the hole in the rubber bushing of the bottle, and the beads were permitted to run in. Glass beads were used at first. These chip and break to an extraordinary extent and in addition are difficult to empty from tube to bottle. We then used stainless steel ball bearings, of three-sixteenths inch diameter, and about 175 to 185 in each tube. The glass beads, however, are less expensive than these metal ones and filter as well. The beads of either type form a layer an inch or more thick above the outlet holes and through this maze clots must find their way in order to descend through the tubing. Large clots are caught on the surface of the beads, small clots are trapped in the column of beads. The outlet holes are a few millimeters above the inside of the rubber stopper, and this difference is enough to hold any glass dust or chips which may settle out during the transfusion. None appeared to go through the tubing in experiments in which, with the use of old chipped glass beads, all the blood emerging from the needle was collected in a vessel and repeatedly diluted with water, decanted and finally examined for glass. Figure 9 shows the method of using the steel ball bearings at present employed. The small filter chamber is of pyrex glass. There is a tapered inlet just large enough for the bearings and an outlet consisting of two holes on the side of a glass tube projecting upward from the bottom of the chamber. The volume of the chamber is 15 cc., and we employ a quantity of bearings displacing 12 cc.

If desired, a few cubic centimeters of air may be trapped in the chamber, converting the filter inlet into a drip tube.

Figure 14 illustrates one of many similar filtration experiments. Five hundred cc. of 0.85 per cent saline solution was added to a flask of 500 cc. of citrated blood twelve days old. The diluted blood was divided into two equal portions and an even distribution of any clot which might be present assured by repeatedly pouring the blood back and forth. The watch glass labeled *a* contains the clot obtained by running the contents of one of these blood flasks unfiltered through a regular transfusion tubing with glass adapter but no needle. The blood was caught in an Erlenmeyer flask and repeatedly diluted and decanted until only clear water, with the clots pictured, remained. Glass *b* shows all the clot that came from the second half of the blood when the steel bearings were used by the old method.

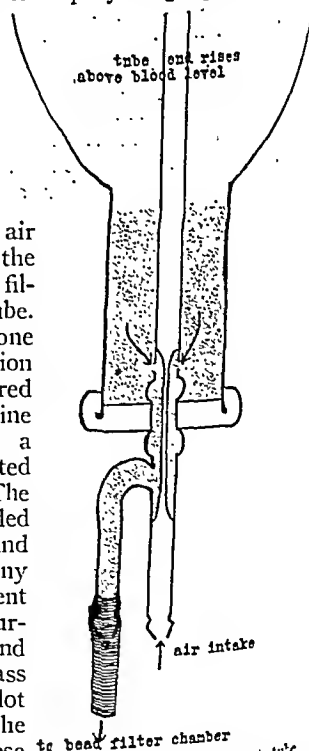


Fig. 13.—Detail of vent tube as used in giving blood. Blood flows through the vent holes and out through the side arm. Air enters through the central channel. Long tube permits the end to be above blood level, avoiding entrance of blood into the central channel.

4. Boland, C. R.; Craig, N. S., and Jacobs, A. L.: *Lancet* 1: 388-391 (Feb. 18) 1939.

Glass *c* shows the quantity of clot the steel bearings filtered out. The finer dispersion of the clot in glass *a* is due to its having run through a small bore glass adapter, whereas that in glass *c* was washed out of the bottle. The total amount of clot in the 500 cc. of blood is a little greater than the total amount in the three glasses, for the tubing traps some. The amount of clot shown is about average. The new filter is even more effective, for it uses the same number of bearings in a column of smaller cross section and greater height.

The apparatus should be so cleansed and cared for that no transfusion reactions may be attributable to it. The procedure employed removes all fibrin and blood pigment, and in every instance the last operation is a thorough rinsing with a large quantity of freshly distilled water. After each transfusion the set is completely dismantled—the work of a moment, since all joints are secured merely by rubber bands. All apparatus is washed in running tap water, the tubing, vent tubes and adapters being attached to cold water spigots for from ten minutes to half an hour. These parts are then boiled with an excess of sodium carbonate for fifteen minutes, all air having been exhausted from the

which simultaneously percolates a continuous stream of boiling 2 per cent sodium hydroxide through the lumen and bathes the exterior in the same solution. After forty-five minutes of this treatment the tubing is flushed with tap water for ten minutes, washed through with 1 per cent acetic acid, then washed with tap water over night and finally with distilled water.

COMMENT

The plan presented has proved a workable one in the administration of the two banks, white and Negro, which we operate, each supplying the blood for from fifty to sixty transfusions a month. There has been general satisfaction with the functioning of the bank despite the wide range of innovations. A part of the benefit from the bank derives from the standardization of transfusion apparatus and technics in the several services, which had all been divergent, and from the centralization of the preparation and care of apparatus. The apparatus now in use is simpler and safer than that previously in use in any service. The transfusion sets are small but complete, the system is almost entirely closed and the sealing of the bottles is air tight. A

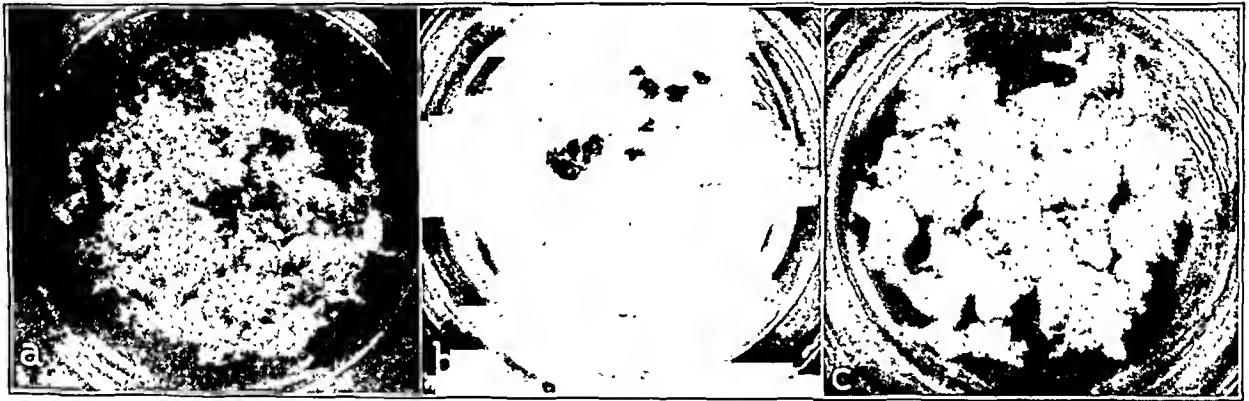


Fig. 14.—Clot contained in 12 day old blood: a, clot recovered from unfiltered half of 500 cc. bottle of 12 day old blood. b, clot recovered from half of 500 cc. bottle of 12 day old blood, filtered through steel ball bearings. c, clot filtered out by the ball bearings.

tubing to permit it to fill with the solution. A forceful stream of tap water is run through again and then a generous quantity of distilled water. The distilled water is obtained fresh daily and its container and the siphon delivery tube are washed daily and cleansed with distilled water. The beads are emptied from the filter chamber by forcing a stream of water through the outlet. The beads are then cleaned like the glassware. Sulfuric acid-potassium dichromate cleaning solution is used for all glassware whenever indicated. The bottles are scrubbed with green soap, then washed in succession with tap water, 4 per cent sodium triphosphate, tap water, 0.5 per cent hydrochloric acid, tap water and distilled water. The rubber bushings and metal caps are scrubbed with green soap, a hand brush being used, and washed with tap water and distilled water. The excess of distilled water is permitted to drain off, and the sets are wrapped and autoclaved within two hours of the time of washing. In the course of the washing the rubber tubing is stretched and squeezed by hand, inch by inch, to loosen any clot. As soon as the tubing is found to have lost its elasticity it is replaced. We use davol, pure gum, black seamless tubing, one-fourth inch by one-sixteenth inch. In the preparation of this tubing it is filled with water, thus expelling all air, and then attached to an apparatus

satisfactory filter has been provided which is efficient without obstructing the flow of blood.

The principal advantage of the bank is, of course, the increased availability of blood. The only criterion for the administration of blood is the patient's need for it. House officers are encouraged to ask the bank for blood at any time, without thought of repayment, since it is our understanding of the function of a blood bank that it must place blood in the category of a biologic therapeutic agent to be used whenever indicated, just as specific serums, hormones or vitamins may be ordered. In many instances the convalescence of patients with low hemoglobin content is hastened by transfusions which augment natural hemopoiesis but which formerly would have been dispensed with as "unnecessary" because of the attendant difficulties. We are also now able to make blood available more rapidly than before. A number of patients owe their lives to this fact.

A recent case offers a dramatic illustration:

At 1:30 a. m. a farmwife aged 17 was brought to the accident room after a 35 mile ambulance drive. She had been known to be more than three months pregnant, had had constant pain the entire period and, with a sudden access of violent pain, had collapsed four days before. After three days of seeming gradual recovery she collapsed again on the day of admission. When seen, she was moribund. She showed air hunger and a

deathly pallor and was almost pulseless. The lower part of the abdomen was rigid, the culdesac was boggy and a large mass involved the left adnexa. With death a matter of minutes we felt justified in administering unmatched group O blood, and within ten minutes of her arrival she was being given a transfusion. With blood still running into her veins she was moved to the operating room, where without interruption she was given a second 500 cc. transfusion during the operation, this time with compatible group A blood. Operation disclosed the expected ruptured tubal pregnancy. During the operation a third transfusion, again with compatible group A blood, was begun, and by the time of its completion the patient's condition had improved gratifyingly. Despite the massive transfusions the hemoglobin content of her blood was still so low the following morning that a fourth 500 cc. transfusion was administered.

The most heroic efforts, under the old conditions, could not have provided this quantity of blood soon enough. The protection of being matched for transfusion can now be more easily extended to a greater number of patients, with no inconvenience or worry to the family in the large number of cases in which transfusion subsequently proves unnecessary. No ward patient need pay for blood from a professional donor because his family can provide no compatible donor. By the same token, the hospital has been spared the considerable cost of transfusions for patients unable to supply donors or to pay the fees of professional donors.

OBSERVATIONS ON 793 CASES OF ACUTE PURULENT OTITIS MEDIA

WITH CHEMOTHERAPY IN 396 CASES

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I have analyzed a series of 793 cases of acute purulent otitis media from my private practice and from the otolaryngologic service of St. Luke's Hospital in the past three years. About 90 per cent of the hospital cases I have seen personally; in about 45 per cent of them the age was 10 years or less, making a fairly equal number of children and adults. It should be noted that St. Luke's is a general hospital, that many of the patients in the series were admitted because of other medical conditions which were complicated by otitis, and that the presence of other pathologic conditions always makes otitis more severe, more prolonged and more difficult to cure.

Before proceeding to my series of 793 cases of otitis media, it may be interesting to trace the incidence of mastoidectomies for the past ten years, in an effort to discover the influence of chemotherapy (chart 1). The year 1930 (ninety-five mastoidectomies) would seem fairly comparable with 1937 (ninety-two mastoidectomies).

It is somewhat difficult to arrive at the correct incidence regarding the years 1937, 1938 and 1939. My impression is that in 1937 the ear infections were comparatively mild, while in 1938 and the first nine months of 1939 they were far more virulent. Hence the drop in the number of mastoidectomies in 1938 seems to me even more significant than the figures indicate.

Of the total 793 cases, in 599 recovery occurred without operation; of this number 231 were selected because of their short duration and because myringotomies could be performed in the hospital, where the condi-

tion of the ears could be observed daily until the discharge ceased. The average duration of discharge in the 113 cases in which chemotherapy was received was nine days; in the 118 in which it was not received the duration of discharge averaged seventeen days. Thus it would seem that chemotherapy reduced the duration of discharge by about 50 per cent and increased the number of recoveries from 67 to 81 per cent.

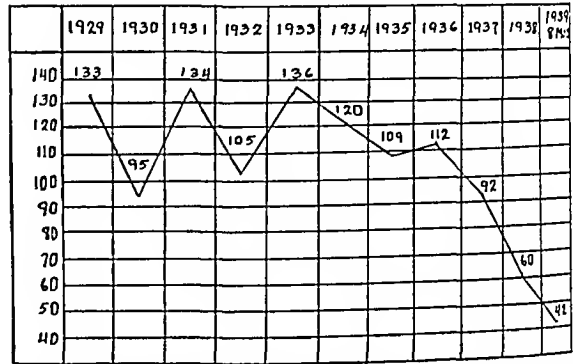


Chart 1.—Distribution of 1,138 mastoidectomies in a ten year period (lacking four months in 1939). This shows a marked drop since 1936, when chemotherapy seems to have changed the picture.

Mastoidectomy was performed in 194 (24 per cent) of the 793 cases of acute purulent otitis media in the hospital (chart 3). Since many of the patients were admitted in an emergency condition, or had had mastoiditis for days or weeks before admission, or were very ill with other diseases on admission, and had had chemotherapy of unknown quantity before admission, a selection was made of 387 cases, in none of which the ear condition was of more than a few days duration. Of these 387 cases, in 207 the condition was treated with chemotherapy and in twelve (5.7 per cent) mastoidectomy was necessary; in 180 the condition were not so treated, and of these twenty-four (11 per cent) came to mastoidectomy. This would indicate that when the drug is given early, before mastoid softening has taken place, the number of cases requiring operation is reduced one half. Incidentally, it shows that of cases properly treated 11 per cent required mastoidectomy while of those taken as they came 24 per cent required it. This is a reduction of over 50 per cent.

BACTERIOLOGY

The bacteriologic study of mastoiditis is not always satisfactory. Culture of material taken at operation showed the various bacteria occurring in the following proportions:

Streptococcus haemolyticus	52 per cent
Nonhemolytic streptococcus	10 per cent
Pneumococcus group III	5 per cent
Staphylococcus	15 per cent
No growth	18 per cent

Although 18 per cent of the cultures were negative, infection was present in the mastoid in all these cases; frequently the applicator was covered with pure pus from the mastoid cavity. There were also reports of "no growth" from pure pus in nasal cultures. In such cases the organisms must have been inert or have become anaerobic at the places from which cultures were taken. Again, it is not uncommon to obtain a culture of staphylococcus or streptococcus from the ear and later find pneumococcus group III in the mastoid culture. It has also been noted in sinus infections that

while the culture from the nose may show *Staphylococcus albus*, the organism in the membrane removed at operation may be *Streptococcus viridans* or *Streptococcus haemolyticus*.

Fifteen per cent of the mastoid cultures were reported to show staphylococcus. This is hard to understand, for in all my experience I have seen only three cases in which I felt justified in calling the condition staphylococcic mastoiditis. In these the cells were filled with thick, tenacious pus similar to that seen in a carbuncle; there was a sharp demarcation at the inner plate, to such a degree that the cells with their contained cones of pus came out as a single mass, leaving the inner table clean as though it had been dissected free. I do not know how to explain this 15 per cent unless it is a question of mixed infection in which the staphylococcus outgrew the more serious organism, or unless it was due to contamination in transmission. *Staphylococcus* is so frequently present in the external auditory canal that a culture taken with a swab is unreliable even when the canal has been treated with alcohol. Culture taken from the knife is far more reliable. Some doctors believe that there is a staphylococcic mastoiditis, much resembling a staphylococcic bacteremia, very resistant to treatment, requiring several operations before complete recovery. However, to me it seems probable that the greater part of the 15 per cent staphylococci and the 18 per cent "no growth" in the tabulation really represent streptococci with a few pneumococci of group III. If this is correct, it is evident that more mastoiditis is caused by streptococci than is shown in this tabulation and that if the ear culture shows no growth or a growth of staphylococci, it is justifiable to resort to chemotherapy in the presence of a severe clinical picture regardless of the bacteriologic data.

COMPLICATIONS IN 194 MASTOIDECTOMIES

No deaths occurred when the mastoiditis had been uncomplicated on admission.

There were two deaths from meningitis. Both patients on admission to the hospital had fulminating meningitis with lateral sinus thrombosis. One of them, with a *Streptococcus haemolyticus* infection, was operated on and received 218 grains (14 Gm.) of sulfanilamide; the other, with a pneumococcus group III infection was operated on, received 120 grains (8 Gm.) of sulfanilamide by Levine tube and died within twenty-four hours.

In one case of sinus thrombosis, double mastoiditis, cloudy spinal fluid, facial paralysis on the right and paralysis of the left sixth nerve, all present on admission, the invading organism was pneumococcus group III. Sulfanilamide was given the week preceding hospitalization, for pneumonia, and again during the first few days following operation. Papilledema persisted for over two months postoperatively; in this case recovery occurred.

In one case of petrositis, sixth nerve paralysis and cloudy spinal fluid (1,300 cells; 62 per cent polymorphonuclears in spinal fluid) recovery followed operation and chemotherapy. In this case culture of material from the ear showed nonhemolytic streptococci; from the mastoid, no growth; a smear from the spinal fluid showed gram-negative cocci.

Two cases of labyrinthitis responded well to chemotherapy. In one case of facial paralysis, occurring two weeks after operation, recovery took place.

There were also three cases of retropharyngeal abscess, two cases of parotid abscess and forty-nine cases of pansinusitis.

In order to illustrate the deceiving picture produced by chemotherapy, I will briefly mention some experiences:

Early in my experience with sulfanilamide, four patients with hemolytic streptococcus infection, in which

immediate operation seemed indicated, were given the drug for twenty-four hours. At the end of this time they were so much improved that operation was deferred. The middle ear entirely cleared up within a week; there was no mastoid tenderness or fever and x-ray examination showed no breaking down. The patients were therefore discharged as cured, with great jubilation. Within ten days three of the four returned with a temperature of 104 F. and the middle ear again in very bad condition. Mastoidectomy in each case revealed a large perisinus and epidural abscess; the remainder of the mastoid cells were filled with granulations and softened bone. With these experiences in mind I have continued the use of sulfanilamide for a full week after symptoms have disappeared and since

doing so have had no such recurrence. However, these cases illustrate the danger of temporizing with mastoiditis when the aural condition indicates mastoidectomy.

In my series of 194 mastoidectomies, recovery occurred in 192 which were uncomplicated on admission. Death occurred in two of the six complicated cases. It is evident from these figures that mastoidectomy is a safe procedure. It is equally evident that complicated mastoiditis is a dangerous condition. One must conclude that it is safer to operate, when the indications are strong, than to depend on chemotherapy.

Mrs. de M. had undoubted mastoid involvement, the roentgenogram showing marked cloudiness. The invad-

	1937	1938	1939 8 Mos.
220		218	
210			
200			
190	194		187
180			
	67%	78%	81%

Chart 2.—Distribution of recoveries without operation in a three year period. Of 793 cases of acute purulent otitis media, in 599 recovery occurred without operation. The average duration of discharge following myringotomy on 231 ears was nine days for 113 ears with chemotherapy and seventeen days for 118 ears without chemotherapy. It would seem that chemotherapy reduced the duration of discharge 50 per cent, and the number of recoveries increased from 67 to 81 per cent.

	1937	1938	1939 8 Mos.
100	92		
90			
80			
70			
60		60	
50			
40			42
	32%	21%	18%

Chart 3.—Distribution of mastoidectomies in a three year period. There were 194, or 24 per cent, mastoidectomies in 793 cases of acute purulent otitis media—a diminution from 32 to 18 per cent in three years. There were 387 myringotomies done in the hospital for acute purulent otitis media of not over two days' duration; of 207 with chemotherapy was done, or 5.7 per cent, mastoidectomy was done, or 11 per cent, mastoidectomy was done. It would seem that infected middle ears which were opened promptly and treated by chemotherapy responded 50 per cent better than those not given chemotherapy. (Incidentally, it shows that of the cases properly treated 11 per cent required mastoidectomy; while of those taken as they came, 24 per cent required mastoidectomy, a diminution of over 50 per cent being due to proper treatment.)

ing organism was pneumococcus of group III. Sulfapyridine was given but, as it caused severe nausea and vomiting, sulfanilamide was substituted. The middle ear cleared up and the drum returned to normal. Operation was advised but the patient preferred to take a chance without it. During the following seven months she was able to live her normal life, but she experienced so much discomfort from the sensation of fullness in the ear and vertigo that she regretted her decision to forego operation. Another x-ray study, eight months after the onset of the infection, showed what appeared to be an abscess cavity in the mastoid picture. The patient now agreed to an operation. No abscess cavity was found; the cells had thickened membrane and were softer than normal; the large cells posterior to the sinus had thickened membrane and considerable new bone formation. The antrum was walled off by hard bone. This case is an apt illustration of the difficulties of diagnosis when chemotherapy is used. The appearance at operation indicated that the lesions in the mastoid would probably have resolved without operation, yet there was persistent discomfort and vertigo for eight months during which period there was always danger of a fulminating meningitis. The x-ray examination before the operation showed what was apparently an abscess.

Since the advent of chemotherapy streptococcal mastoiditis may be just as misleading as that caused by pneumococcus group III. That is, the clinical picture may indicate improvement while the mastoid bone is being seriously involved with very few symptoms to show it. This may be due to the fact that the drug acts best in very vascular areas, such as the middle ear, but is not effective in an area where the circulation is poor, such as a necrotic area in bone. Whatever the reason, chemotherapy causes the clinical picture in other types of mastoiditis to resemble that caused by pneumococcus group III.

My most dramatic experiences have been in connection with pneumococcus group III. It is indeed fortunate that this organism does not appear more often (5 per cent) as it produces the most deceptive form of mastoiditis. When sulfanilamide is given in these cases, the picture is still further complicated, making the condition even more dangerous and difficult. Even without the drug, this infection will often appear to yield to treatment while the lesion in the mastoid is really increasing. Furthermore, the presence of mastoiditis may not even be suspected prior to the onset of meningitis. I have seen a considerable number of cases of acute purulent otitis media due to this organism in which recovery occurred under chemotherapy, but when this infection is present in an acute ear condition it is not safe to assume that recovery will occur for at least a month, even though the drum and hearing return to normal. The following cases illustrate the typical clinical course of pneumococcus group III infections of the middle ear:

A previously described patient, J. M.,¹ had a myringotomy which showed pneumococcus group III in both middle ears. In about two weeks the infection cleared up and drums and hearing returned to normal. About four weeks later facial paralysis developed on the right side. Roentgenograms showed only a slight cloudiness of the right mastoid. Culture from the right mastoid at operation showed "no growth," although the cells were filled with granulations. Symptoms of labyrinthitis developed, with restlessness, Kernig's sign and opisthotonos; the spinal fluid showed 360 cells. An abscess was

found in the petrous bone, from which pneumococcus group III was obtained, although the mastoid culture had been sterile. This patient recovered. It must be noted that in this case the drum membrane and hearing had returned to normal. The present use of chemotherapy may produce a similar situation in any infection of the middle ear.

J. R. M., a child, was very ill with pneumonia and was given chemotherapy for that condition. A swelling appeared behind the right ear, and the following day there was discharge from both ears. The pneumonia in this case was apparently regarded as more important than the ear condition, as there was no complaint about the latter. The child, with a temperature about normal, had double mastoiditis and right sinus thrombosis, with facial paralysis on the right, paralysis of the left sixth nerve, marked nystagmus, opisthotonos and a double Kernig sign. Culture revealed pneumococcus group III.

In pneumonia there is seldom any complaint of pain in the ears even though they are full of pus. This is doubly true when chemotherapy is used, as the drug seems to have some analgesic effect and, with the present treatment, one may therefore expect a picture similar to the pictures just presented, not only with pneumococcus but with any organism found in the middle ear.

These experiences lead to the conclusion that chemotherapy is of decided advantage in the treatment of acute purulent otitis media provided it is started early, before the condition of the mastoid has progressed to softening of the bone. Where such softening has occurred, the use of chemotherapy so changes the clinical picture as to make it almost impossible to determine the presence of progressive bone destruction and to ascertain the advisability of operating. The clinical picture is still by far the most reliable guide to pathologic conditions in the mastoid, although roentgenograms are an invaluable aid and at times afford the only diagnostic sign. In doubtful cases it is well to stop administration of the drug for a time in order to get the true clinical picture.

CHEMOTHERAPY AS USED IN THIS SERIES

At first chemotherapy was used with great caution, the drug being stopped at the first sign of toxicity. My associates and I obtained some marvelous results in adults with a dosage of 10 grains (0.65 Gm.) of sulfanilamide four times a day—a total of 40 grains (2.6 Gm.). Later we gave 10 grains with sodium bicarbonate every four hours, day and night. Much less attention was paid to unpleasant symptoms. The results were even more beneficial. Today, our general rule for dosage is to give during the twenty-four hour period an amount totaling slightly less than 1 grain (0.06 Gm.) per pound of body weight up to 90 pounds (41 Kg.). During the first twenty-four hour period we double, triple or quadruple the amount for the first two or three doses, depending on the severity of the infection and the type of patient. As to the form of the drug used, our preference is for sulfanilamide. It is, of course, essential to watch the urine and blood carefully. At first a daily blood count is taken; later, if no bad effects are observed, the interval is lengthened to once in two days while the drug is being taken, with an additional count one week after it has been discontinued.

In the beginning sulfanilamide was used; later azosulfamide was substituted but with less good results. Sulfapyridine was used for pneumococcus group III infections, successfully in a number of very severe cases of otitis media. However, the symptoms caused by the latter drug, such as headache, disorientation, delirium and vomiting (simulating meningitis) or vertigo (simulating labyrinthitis) resemble so closely the syndrome

1. Bowers, W. C.: Two Cases of Petrous Bone Abscess, *Laryngoscope* 28:412 (June) 1928.

of complicated mastoiditis that we were forced in some cases to discontinue its use in order to differentiate. In some such cases sulfanilamide was substituted, with occasional improvement of the symptoms.

We have had no permanent ill effects, despite the fact that not infrequently we have seen the cell count and hemoglobin drop alarmingly. In such cases there has always been quick response to discontinuance of the drug and to blood transfusions.

INDICATIONS FOR CHEMOTHERAPY

Chemotherapy is indicated if, at the time of myringotomy, the fundus has a very bad appearance or if myringotomy reveals pus or fluid under great pressure, with or without the presence of mastoid tenderness and regardless of the results of culture. Chances of prompt resolution are 50 per cent improved and the chances of operation are 50 per cent diminished by the use of the drug.

If the fundus does not seem to be in bad condition and the pressure on myringotomy is not great, chemotherapy may be deferred, but if subsequently the ear does not improve promptly chemotherapy should be started at once, regardless of the culture. If complications intervene, the drug should be used immediately regardless of culture, but never without removing the focus. If there is doubt about the situation, the drug should be temporarily discontinued in order to get the correct clinical picture.

After mastoidectomy the wound should be free from pus and the temperature should return to normal within two or three days. If sulfanilamide is given during this early postoperative period and the fever persists, accompanied by symptoms simulating meningitis or labyrinthitis, the picture is very alarming. For this reason, it is preferable not to give the drug postoperatively in uncomplicated mastoiditis.

The drug is not effective in uncomplicated chronic mastoiditis or in cases in which there have been previous severe attacks of acute purulent otitis in the same ear. The drug must be continued for at least one week after the disappearance of all aural symptoms.

The practice of giving chemotherapy without proper supervision of blood and urine cannot be too strongly condemned. During administration of the drug there should, as a rule, be daily examinations of the blood—never less frequent than every two days—and a final examination should always be made one week after the drug has been discontinued.

CONCLUSIONS

As a result of my experience in the treatment of this series of cases, I have arrived at the following conclusions: If chemotherapy is given early, before bone destruction occurs, the duration of discharge is diminished by about 50 per cent and the number of mastoidectomies is diminished by about 50 per cent.

When the clinical picture strongly suggests mastoidectomy, it is safer to operate.

After uncomplicated mastoidectomy, it is better not to give the drug.

Complicated mastoiditis requires intensive chemotherapy.

At times it is necessary to stop the drug in order to obtain the true picture, as the drug cures the middle ear while progressive bone destruction is taking place in the mastoid.

Chemotherapy has unquestionably added greatly to the confidence of physicians in their ability to conquer acute otitis media and mastoiditis. They have always

been apprehensive of meningitis as long as the ear continued to discharge.² In the twenty-five years prior to 1936, only seventy-six recoveries from streptococcic meningitis were reported in the literature; since 1936 over 200 recoveries have been reported. Mortality has dropped from 97 to 35 per cent. This is a great comfort and a signal achievement. Yet one should be ever mindful of the fact that chemotherapy may also so obscure the clinical picture that there is an increased danger of the unheralded sudden onset of grave complications, such as meningitis, and that all the symptoms of mastoiditis may disappear under the influence of these drugs, while the lesion is actually spreading.

Pasteur has said "There is no peril in expressing ideas a priori when they are taken as such and can be gradually modified, perhaps even completely transformed according to the result of the observation of facts." In experiments with chemotherapy one is justified in stating that its beneficial results are now established beyond the a priori state, but observations must still be continued with minds open to every possibility of modification and transformation. Another valuable aid to the practice of otolaryngology has been found, but an aid which has changed the clinical picture of mastoiditis and its complications so much that it produces a false sense of security and demands a new interpretation of the clinical picture.

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THE USE OF ZINC PEROXIDE IN MALIGNANT LESIONS

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Keeping a patient with a necrosing carcinomatous ulcer free from exudate and foul odor is a well known problem in the hospital and at home. All surface ulcers are infected to some degree. The cancer necrosis should not be blamed altogether for the foul odor and profuse discharge. The combination of necrotic cancerous tissue and infected tissue is responsible. Treatment should aim not only to eradicate the neoplastic growth but also to disinfect and deodorize the lesion. The abundant necrotic tissue, the poor blood supply and the inadequate drainage offer an excellent opportunity for growth of organisms. Postirradiation lymphedema, fibrosis and endarteritis add to the devitalization of the tissue. The usual methods of antisepsis in conjunction with surgical excision and irradiation may suffice to control a large percentage of carcinomatous ulcers, but some advanced lesions, in the face of constant treatment, become steadily worse and are given up as hopeless. This report is concerned with the latter group.

These lesions are usually deep radionecrotic ulcers with or without residual malignancy. Histologic descriptions of radionecrotic lesions include scanty polymorphonuclear reaction, macrophage infiltration, progressive scarring with dense acellular fibrous and elastic tissue and progressive endarteritis obliterans. Grossly, the striking features are the chronicity of the lesion, the firmly fixed and deeply anchored central

2. Anderson, E. D.: Hemolytic Streptococcus Meningitis, *J. A. M. A.* 108:1591 (May 8) 1937. Gray, H. J.: Streptococcic Meningitis, *J. A. M. A.* 105:92 (July 13) 1935.
From the Tumor Clinic and Tumor Research Unit, Veterans Administration Facility. Published with the permission of the Medical Director of the Veterans' Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

slough, the atrophic anemic granulations and a thin coat of fibrin covering all.¹

Meleney's work on the use of zinc peroxide in the successful treatment of phagedenic ulcers, foul mouth and neck infections and other specific types of gangrene stimulated us to apply this substance to exudative

element of infection is present, further sloughing occurs. Infection invariably accompanies necrosis, and the absorption of toxins from the ulcer is a large factor in the debility, malaise and cachexia. To care for the patient, the infection must be considered, whether or not residual neoplastic activity is present. Ashhurst⁴ has stated that patients frequently have died of sepsis arising in the ulcerated surface of a malignant tumor while the tumor itself had very little to do with it. Moreover, radiologists have noted that infected tissues have decreased radium sensitivity.

Bacteriology of Thirty-Five Nonhealing Radionecrotic Ulcers During Routine "Antiseptic" Treatment Before Institution of Zinc Peroxide Dressing

Organism	Occurrence in 18 Lesions Connected with Intra-Oral Cavities	Occurrence in 17 External Lesions	Total
Streptococci, anaerobic or micro-aerophilic	13	13	26
Streptococci, aerobic	0	4	4
B. necrophorus	10	8	18
B. fusiformis	14	1	15
Staphylococcus aureus	6	7	13
Staphylococcus albus	2	1	3
Diphtheroids	11	2	13
B. pyocyaneus	0	7	7
E. coli	0	4	4
Yeast	5	2	7



Fig. 1 (case 1).—Recurrence of palatal neoplasm.

The management of these cases affords difficult problems because of the chronicity of the ulcer, the associated pain while sloughs are present, the difficulty in controlling infection while necrotic tissue remains, the

necrosing lesions of cancer on the body surface. The properties of zinc peroxide have been well established by the writings of Meleney.² It will suffice to state that zinc peroxide is a preparation which when suspended in distilled water liberates and maintains for a prolonged period a constant potential of oxygen having a definite bactericidal action in vitro and in vivo on certain anaerobic and micro-aerophilic organisms, as well as aerobic hemolytic streptococci and pneumococci.

Infection following radionecrosis results in delayed healing and subsequent necrosis of the granulation tissue making it a factor of great importance. Phemister³ has shown that bone killed by irradiation, if kept in normal function and free of infection, will act much as a bone graft. If injury, loss of function or infection takes place, that portion of the bone is sequestered. The picture is similar with tendon and cartilage. If conditions are aseptic, a slow repair will take place. If any



(Fig. 2 (case 1).—Immediately after irradiation.

toxemia and the very foul odor. Radical excision is obviously the treatment of choice,⁵ but because of the extent of the ulcer, the situation and the patient's general condition, often this cannot be done.

4. Ashhurst, A. P. C.: Surgical Conception of Malignant Disease, in Nelson's New Loose-Leaf Surgery, New York, Thomas Nelson & Son, 1937, vol. 2, p. 155.
5. Davis, J. S.: Clinical Illustrations of Deep Roentgen-Ray and Radium Burns, Am. J. Roentgenol. 20: 43-78 (Jan.) 1933.

1. Scott, R. K.: Radionecrosis: A Clinical Study, M. J. Australia 2: 1-8 (July 7) 1934. Wright, R. D.: Pathological Manifestations in Radionecrosis, ibid. 2: 8-14 (July 7) 1934. Wollach, S. B.: A Summary of the Effects of Repeated X-Ray Exposures on the Human Skin, Am. J. Roentgenol. 13: 139-143 (Feb.) 1925.
2. Meleney, F. L.: Zinc Peroxide in the Treatment of Micro-Aerophilic and Anaerobic Infections with Special Reference to a Group of Chronic Ulcerative, Burrowing, Nongangrenous Lesions of the Abdominal Wall, Ann. Surg. 101: 997-1011 (April) 1935; Zinc Peroxide in Surgical Infections, S. Clin. North America 16: 691-711 (June) 1936. Meleney, F. L., and Johnson, B. A.: The Prophylactic and Active Treatment of Surgical Infections with Zinc Peroxide, Surg., Gynec. & Obst. 64: 387-392 (Feb., No. 2 A) 1937; Further Laboratory and Clinical Experiences in the Treatment of Chronic, Undermining, Burrowing Ulcers with Zinc Peroxide, Surgery 1: 169-221 (Feb.) 1937. Meleney, F. L.: The Use of Zinc Peroxide in Oral Surgery, Internat. J. Ortho. 23: 932-940 (Sept.) 1937; The Prophylactic and Active Use of Zinc Peroxide in Foul-Smelling Mouth and Neck Infections, Ann. Surg. 107: 32-38 (Jan.) 1938. Johnson, B. A., and Meleney, F. L.: The Antiseptic and Detoxifying Action of Zinc Peroxide on Certain Surgical Aerobic, Anaerobic and Micro-Aerophilic Bacteria, ibid. 100: 881-911 (June) 1939.
3. Phemister, D. B.: Radium Necrosis of Bone, Am. J. Roentgenol. 16: 340-348 (Oct.) 1926.

Bacterial synergism has been demonstrated in the laboratory and observed clinically.⁶ Physicians have recognized that mixed infections despite their frequent "nonpathogenic" organisms are more serious than infections with but a single-species of organism. Conversely, clinicians have observed that serious infections, espe-



Fig. 3 (case 1).—After treatment with zinc peroxide, showing well defined ulcers and freedom from slough.

cially those involving necrotic and phagedenic lesions, yield more than one species. The combination of certain species of bacteria performing certain functions which neither can perform alone has been called synergism. Virulence may be enhanced; nonpathogenic species in combination may become virulent. Nonhealing ulcers show a variety of organisms, not a few of which may be regarded as saprophytes. Synergistic action should be kept in mind in studying tissues in which mixtures of organisms are frequently found.

Thirty-five radionecrotic ulcers with and without persistent malignancy were studied bacteriologically. Anaerobic as well as aerobic studies were made. Only those ulcers were selected which were under routine antiseptic treatment but remained foul, necrotic and painful and showed no evidence of healing. In every instance more than one organism was found.

The lesions may be divided into eighteen connected with the oral mucous membrane—palate, sinuses, alveolar ridge, tongue, floor of mouth, tonsil, or external lesions with intra-oral extension—and seventeen external lesions of the body surface not so connected. The only bacteriologic difference between the intra-oral and external lesions was the presence of *Bacillus fusiformis* and diphtheroids in the former and of *Escherichia coli* or *Bacillus pyocyaneus* in the latter.

Anaerobic or micro-aerophilic streptococci were found in twenty-six lesions. Of these five were hemolytic. Aerobic streptococci, all nonhemolytic, were found in four lesions, all external. *Bacillus necrophorus* was found in eighteen cases, of which six showed hemolysis. *Bacillus fusiformis* was found in fifteen lesions. Only one intra-oral lesion contained neither *B. necrophorus* nor *B. fusiformis*. This had an almost pure culture of anaerobic nonhemolytic streptococci. The most frequent combinations were anaerobic nonhemolytic streptococcus and *B. necrophorus* with either *B. fusiformis* and diphtheroids in the oral lesions, or with staphylococcus and *B. pyocyaneus* in the external lesions. Cultures were made during the course of treatment and it was noted that the anaerobes were the first to disappear, but after the zinc peroxide dressing had

been omitted for from three to seven days they were the first to reappear.

The odor disappeared on the application of zinc peroxide⁷ but reappeared if the dressing was omitted for a few days. If the dressing was applied for two weeks, from three to seven days was necessary for the reappearance of the characteristic odor and the positive anaerobic cultures. Early in the course of study we found that lesions without odor had a negative anaerobic culture.

The method of application of zinc peroxide is more fully described in several of Meleney's articles. The wound is cleaned with peroxide and saline sprays, free necrotic tissue is gently removed, and the wound is again sprayed. A preparation of zinc peroxide (previously sterilized by baking at 140 C. for four hours in a dry oven) is mixed with an equivalent amount of sterile distilled water and mixed thoroughly with an aseptic syringe. More water is added until the paste has a consistency of about 40 per cent cream, and this is applied by the syringe to the entire lesion. Fine mesh gauze is soaked in the suspension and applied throughout the lesion and into all the sinuses and interstices of the wound. The whole is covered with sterile pads soaked in distilled water and the wound is packed against evaporation with several layers of petrolatum or zinc oxide gauze. The dressing is secured by a larger pad and bandages. At no time has it been necessary to dress a wound twice in one day; occasionally dressings have remained on for forty-eight hours. If the patient is to receive irradiation, the wound is mechanically cleaned with peroxide and saline solution, and sterile



Fig. 4 (case 2).—Postirradiation ulcer after treatment with zinc peroxide. Note absence of slough, epithelizing of nuchal region and sharply delimited edges.

saline packs are placed for protection before treatment. After irradiation the wound is irrigated and zinc peroxide is applied. Because of the evident possibility of secondary irradiation from any zinc salt remaining in

6. Meleney, F. L.: Bacterial Synergism in Disease Processes, *Ann. Surg.* 94: 961-979 (Dec.) 1931.

7. After disappointing results with other products, we have used only the special medicinal brand of zinc peroxide, Z. P. O., of Merek & Co., Inc. This product has not yet been considered by the Council on Pharmacy and Chemistry of the American Medical Association.

the wound, it is necessary to use large quantities of fluid and to insist on complete removal of all particles of zinc peroxide before the patient receives his irradiation. (In some cases it is next to impossible to wash off all the zinc peroxide, but to date no abnormal changes have been noted after irradiation.)



Fig. 5 (case 3).—Postirradiation lesion four days after beginning of zinc peroxide treatment. The original lesion showed necrotic tissue at both upper and lower lesions level with the skin. At this time trismus was still present.

In the treatment of oral lesions (lesions of the cheek, tongue, gums, floor of mouth and palate) and bone necroses, the zinc peroxide is applied as a thick paste every three hours and a 1 to 3 suspension is used as a mouth wash. Before and after meals the lesion is washed with sterile saline solution. When trismus is present, as in several cases of radionecrosis following irradiation of carcinoma of the alveolar ridge, we have found it advantageous to apply the zinc peroxide cream using as a syringe a large bore glass drinking tube attached to a bulb. Throat lesions receive a spray of a 1 to 2 suspension and again a paste is directly applied to the lesion. These are reapplied as often as necessary. As Wintrup⁸ suggested, we have advised patients not to swallow the preparation. However, several have done so and have reported no ill effects either immediate or late, although Meleney has noted occasional mild nausea.⁹

In lip and mouth cancers, while the patient is receiving his preoperative dental prophylaxis, we have been using zinc peroxide as a mouth wash. This has not been continued during the irradiation period because of the possible danger of secondary irradiation, as it is very difficult to remove zinc peroxide from between the teeth. Immediately after the course of irradiation has been completed, the patient is placed on routine treatment with zinc peroxide mouth washes. No definite data as to the prevention or mitigation of radionecrosis have as yet been obtained.

8. Wintrup, J. P.: Preliminary Report on Use of Zinc Peroxide in Mouth Infections. *Surgery* 4: 124-131 (July) 1938.
9. Meleney, F. L.: Personal communication to the author.

REPORT OF CASES

CASE 1.—C. M. had previously been treated at the Tumor Clinic for a squamous carcinoma (nonkeratinizing) of the hard palate with a total of 7,300 roentgens through ports directed to the right and left side of the face and through a mouth cone. Four months later a recurrence at the posterior aspect of the tumor was noted, and five radon seeds totaling 746 millicurie hours were inserted. Two weeks after the implantation there was noted a steady dull pain in the palate. Progressive increase in the pain caused the patient to apply for admission, stating that for the preceding month he had been unable to eat or sleep.

An extremely tender deep necrotic ulcer measuring 1 by 3 cm. and extending into the left maxillary sinus was noted. There was a very fetid odor despite all attempts at mouth hygiene, and the patient required large doses of sedatives. No recurrence of the carcinoma was found, and when a culture showed the presence of *B. necrophorus*, anaerobic streptococci, diphtheroids and *B. fusiformis*, zinc peroxide paste was applied three times daily plus a mild mouth wash. After two days all sedatives were withdrawn and the patient had no pain or odor and slept and ate well. On discharge two weeks later, the lesion had sharply defined margins, was nontender and had no odor. Healthy granulations appeared at the border. Instructions were given to continue zinc peroxide paste at home.

CASE 2.—H. L. R., for a basal cell carcinoma arising on the nuchal region, had received irregular roentgen and surgical treatment, type unspecified, for ten years. On admission to the Veterans Administration Facility the patient presented a 12.5 by 7 cm. deeply ulcerated lesion on the nuchal and supra-



Fig. 6 (case 3).—Ten days after the first application of zinc peroxide dressings; no odor was present. The defect opened into the oral cavity.

spinous areas. In 1937 a block excision was done and radon seeds were implanted totaling 2,870 millicurie hours because the excision was thought to be incomplete, as the tumor infiltrated near the apex of the lung around the brachial plexus and the subclavian vein. A total of 21,600 roentgens was given over a period of four months.

In March 1939 the patient was readmitted with complaints of inability to move his neck, severe pain of the entire left

shoulder and neck, loss of 20 pounds (9 Kg.) and general malaise. Recurrence of the nuchal margin was excised with a Bovie, and a typical massive foul ulcer which extended to the scapula was given azochloramid dressings three times daily. No change was noted for four months, and culture showed *B. necrophorus*, anaerobic streptococci and a few staphylococci. Zinc peroxide dressings were instituted, and two weeks later



Fig. 7 (case 3).—Ten days after the start of treatment, showing absence of trismus.

the lesion showed no evidence of odor, healthy granulations were filling in the ulcer and the patient could move his neck freely. One month later the reentrant angle was completely filled in, the scapula was entirely covered with healthy granulations, and the nuchal portions of the wound were epithelized. Biopsies have been negative, and the patient is awaiting plastic reconstruction.

CASE 3.—A. P. R., after a creosote burn of the face and mouth in February 1932, complained of dryness of the lips and an elevation on the lower lip. After several electrodesiccations he was referred to this hospital and in February 1933, after a diagnosis of keratinizing squamous cell carcinoma of the lower lip on the right, he was given 900 millicurie hours by external pack, radon implants totaling 400 millicurie hours and 16,000 millicurie hours to the cervical regions bilaterally. This was completed March 7, 1933, and the patient was discharged.

Follow-up appearances were normal, but on March 3, 1939, he was admitted for what proved to be a keratinizing squamous cell carcinoma on the right lower alveolar ridge with extension to the buccal mucosa. At this time he received 3,450 roentgens of high voltage x-rays to the right side of the face and 1,550 roentgens to the face and neck on the right. There was a persistent lesion on the buccal mucosa, and on May 5 radon implants totaling 952 millicurie hours were given and the patient was discharged.

The follow-up appearance through September was normal, but in October the patient had pain in the mandible and was seen by a local radiologist, who instituted fifteen treatments of undetermined dosage in as many days, using a hundred kilovolt machine. One month after the irradiation, the entire right half of the face swelled and complete trismus was evident. During this period the weight dropped from 257 to 190 pounds (from

117 to 86 Kg.), and large doses of morphine were necessary to control the pain. He was given a few weeks to live.

December 21 the patient was admitted to the Veterans Administration Facility on a stretcher. He looked critically ill and was very weak. He could sip water through a hiatus in his teeth, but a definite trismus was present. On the right cheek there was a foul slough in the plane of the face measuring 4.5 by 3 cm. Below the mandible there was a similar area of slough measuring 2 by 2.5 cm. The odor was so foul that personnel usually quite hardened could barely force themselves to enter the room. Patients in the neighboring wards complained of the "overflow" odor. A culture was taken and zinc peroxide dressings were immediately started. Sloughing necrotic tissue was removed as it appeared free, and zinc peroxide paste was applied by a narrow take to the sloughing buccal surface. The dressings were done daily but the intra-oral paste was applied four times daily. In two days the lesion was fairly well deodorized. In four days the patient felt well enough to be up in a chair to be photographed. The second picture was taken ten days after admission, when the wound was clean, the trismus and tenderness completely gone and the patient free from pain. Culture showed the characteristics of anaerobic saprophytes, and biopsy showed necrotic muscle with large clumps of bacteria. No narcotics have been given since his third day and none have been requested. He has gained 10 pounds (4.5 Kg.), and a peripheral neuritis due to dietary insufficiency has slowly disappeared.

CASE 4.—C. D. was admitted with a history of multiple pilonidal sinuses treated for twenty-one years by serial operations. Two years before entry x-ray examination revealed osteomyelitis of the sacrococcygeal region and the coccyx was removed. One year previously he noted pain, swelling and hemorrhage around the internatal cleft and treated this with salve. Six months before admission pain was so severe that nine roentgen treatments (factors unknown) were given at weekly intervals.

Examination revealed scarring and ulceration of the medial aspect of both buttocks with a $10 \times 5 \times 1$ cm. punched out irregular ragged defect extending to the rectum. Biopsy



Fig. 8 (case 4).—C. D.; postirradiation defect of the buttocks. Note the absence of inflammatory erythema. Residual carcinoma was present at the upper portion. Note the proximity to the anus.

revealed squamous cell carcinoma. The patient was given a total of 5,475 roentgens of superficial x-rays over a period of two months. During the postirradiation period pain became extremely severe, and the patient required large amounts of narcotics. Despite antiseptic treatment with various chlorine compounds, the wound became very foul and the profuse discharge sickened even the patient. Biopsies were done and subacute

and chronic inflammation was reported. The condition progressed and the patient was unable to turn or move without excruciating pain and could tolerate no dressings save nupercaine ointment. Because of the profuse discharge, pads were changed six to seven times daily.

Four months after the course of irradiation, material from the wound was cultured and anaerobic streptococci, *B. necrophorus*, and *B. coli* were obtained. Zinc peroxide dressings were applied once daily. Immediately the drainage ceased and the odor became less pronounced. Cultures made one week after institution of the zinc peroxide therapy revealed non-hemolytic anaerobic streptococci, *B. necrophorus*, and *B. pyocyaneus*. One week later the culture showed only *B. coli*. At this time it was necessary to mix a small amount of butyn with the dressing as the patient complained of burning. This was later discontinued. The slough cleared; the overhanging edges, circumareolar erythema and foul discharge gave place to a deep but sharply delimited ulcer with a clean base on which evident recurrences were seen. Biopsy showed recurrent tumor, and irradiation was again started. Before using zinc peroxide, the patient required one-fourth grain (0.016 Gm.) of morphine every three hours; two weeks later he required codeine at only irregular intervals.

COMMENT

Cultures taken have shown scant or no growth after the lesion has been treated with zinc peroxide for a period of two weeks. This is in accord with the work of Johnson and Meleney,² who found zinc peroxide to be almost specific against the three predominant organisms noted in this study. Twenty-four hours after the first application of zinc peroxide, there was a definite loss of odor in all but one case. Bacteriologic studies showed but little change, and the loss of odor is attributed to oxidation and/or absorption of the bacterial metabolites. Drainage has been markedly lessened. Patients previously requiring from three to seven dressings daily needed but one application of zinc peroxide. Exquisitely tender nonhealing postirradiation ulcers with a surrounding aura of erythema soon showed clearly defined margins, a disappearance of the erythema and loss of hypersensitivity. The necrotic central slough lessened and was easily removed, leaving a clean granulating base. Several lesions previously diagnosed as postirradiation ulcers with initial biopsies showing "acute and chronic inflammation" were given a period of zinc peroxide treatment. After the treatment diagnosis of persistent malignancy was made grossly and verified histologically. Although I have no definite data, it is my impression that the postirradiation ulcers healed more rapidly under zinc peroxide than previously noted.

Pain can be judged only by the amount and frequency of narcotics required. Invariably the dosage and frequency of the narcotics were decreased to an appreciable degree. Most of the patients required nothing but mild sedatives after the regular institution of the zinc peroxide dressing. The freedom from embarrassment and the return to normal social contacts and interests together with newly acquired confidence and hope have been noted uniformly.

SUMMARY

Thirty-five cases of radionecrotic ulcers with and without persistent tumor growth have been studied bacteriologically. A predominance of anaerobic organisms has been observed. Zinc peroxide has been used clinically in these cases with control of fetor, infection and pain. Existing infection in irradiation ulcers may obscure the persistence of tumor tissue not only grossly but histologically. The prophylactic use of zinc peroxide has been undertaken to prevent or diminish the frequency or degree of radiation bone necrosis in lesions of the mucous membrane.

RETRUDED CHINS

CORRECTION BY PLASTIC OPERATION

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AND

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No matter how slight or how marked may be the retrusion of a chin or mandible, such an abnormality invariably disturbs to some degree the function of the jaws and the symmetry or normality of facial contour. Such being the case, it is obvious that in the treatment of any retruded mandible there are two objectives to be considered: the functional and the esthetic. While it is true that many operative methods will accomplish both of these objectives more or less satisfactorily, in this paper we are concerned chiefly with those surgical measures of a purely cosmetic nature which are intended to correct or improve the visible external deformity produced by a retracted mandible.

In recent years the esthetic results attainable by plastic procedures in the treatment of retruded chins are increasingly more satisfactory. We are convinced that such operations, alone or in conjunction with other measures, offer the most desirable results in many cases. However, we do not imply that plastic surgery extends a solution to every problem or even the majority of problems arising in the management of these defects

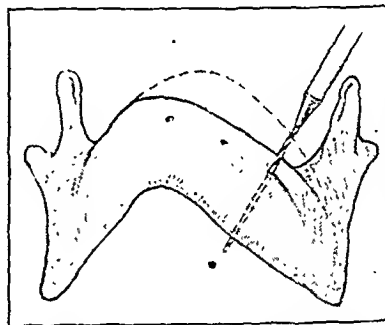


Fig. 1.—Fixation of a large cartilage implant to a retruded mandible in reconstruction of the chin: three holes placed about 1 cm. apart are drilled through the anterior portion of the lower jaw (see figure 2).

of the lower jaw; the fields of orthodontia and oral surgery are indispensable. Even with a comprehensive knowledge of the therapeutic possibilities, the selection of the most suitable method or methods to be employed in correcting a retruded chin is frequently a difficult task. Naturally the choice is dependent on many

factors but primarily on the cause and extent of the deformity and on the age, financial status and personal wishes of the patient.

From an esthetic point of view, one conspicuous fault in some technical procedures designed to correct the external deformity resulting from a retruded chin is the failure of these operations to establish normal dental occlusion. Although we do not wish to engage in a discussion of the dental aspects of the subject, the fact that no other facial deformity is more intimately related to the occlusion of the teeth is worthy of emphasis.

It is well to remember that a significant association exists between dental articulation and facial contour. Embryologic and anatomic studies have shown that the development, eruption and ultimate position of the teeth in the dental arches determine the shape or form of the maxillary bones and, in turn, the conformation of the overlying soft tissues. It is evident, therefore, that the manner in which the dental cusps interlock is

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reflected in the features of every individual; even minor disturbances of occlusion will produce some degree of facial asymmetry or disharmony. In short, no face is perfect in contour unless the teeth are faultless in occlusion.

Very few patients with a retruded chin, regardless of the cause of the deformity, are free from malocclusion; as a matter of fact, the disturbed occlusion is usually most conspicuous. Consequently, one may rightly assume that plastic procedures capable of effecting entirely satisfactory esthetic results not only must produce a natural contour of the chin but also must establish normal articulation of the teeth; at least, such operations must create a semblance to normal dental occlusion.

Much could be written on the psychologic value of correcting facial deformities such as the one under discussion, but the mental satisfaction which some persons experience after a reconstructive operation for a retruded chin is astonishing. There seems to be an inclination among many people to regard a retruded chin as a rather trivial deformity, but whether or not we consider it to be of little consequence does not alter the fact that in the patient's mind the defect is of extreme importance.

ETIOLOGY

A study of the etiologic factors which contribute to the production of a retruded lower jaw requires some familiarity with the physiologic changes that occur in the mandible during its development. As has been previously stated, the contour of the mandible is largely controlled by the growth, eruption and position of the teeth in the dental arches. As each tooth erupts, the jaws progress another step in development by expanding and changing in form to meet the physiologic requirements of support for the tooth when at rest and when subjected to the stresses of mastication. The conformation of the mandible, therefore, is continually being altered until its adult form is attained. Any agent which interferes with the normal forces of tooth eruption marks the beginning of a malocclusion, and all succeeding teeth that erupt occupy an unnatural position in the dental arch; this, of course, provokes an abnormal mandibular contour which is accentuated by the subsequent devel-

opment of the lower jaw. Again, any factor which disturbs or arrests the growth of the mandible not only directly produces some bony deformity but also indirectly misdirects the normal growth of the lower jaw by creating a malocclusion. As a result of this process, the original deformity is increased year by year until the development of the mandible has been completed.

Since the etiologic factors which produce mandibular retrusion occur during the growing period of the individual when the jaws are undergoing a series of changes in development, the primary deformity can be expected to become gradually more pronounced. In most instances, then, a retruded chin or mandible is not a static deformity, which, when once established, remains unchanged; on the contrary, it is one of progressive severity. Not until the physiologic processes of development of teeth and bone have been completed does such a deformity reach its final proportions.

We have found it convenient to catalogue retruded chin and mandible deformities in the following manner: (1) retruded mandibles due to malocclusion, (2) retruded mandibles due primarily to factors which arrest the growth of the lower jaw and secondarily to the subsequent malocclusion, and (3) receding chins not associated with malocclusion.

The first group includes all mandibular retrusions resulting from a malocclusion and characterized by a distal relationship of the lower to the upper dental arches. A retrusion of the lower jaw is always an inevitable sequela of such malposition of the teeth. The common etiologic factors which favor the development of this type of deformity are inheritance, supernumerary teeth, abnormalities of the tongue, early loss of the deciduous teeth, long retention of deciduous teeth, late eruption of the permanent teeth, early loss of the permanent teeth, improper dental restorations, mouth breathing, and habits such as thumb sucking. Other causes are rickets, syphilis and diseases of childhood, which not infrequently upset the normal physiologic processes of growth and eruption of the teeth.

In the second group of retruded mandibles there are two sets of etiologic factors: primary and second-

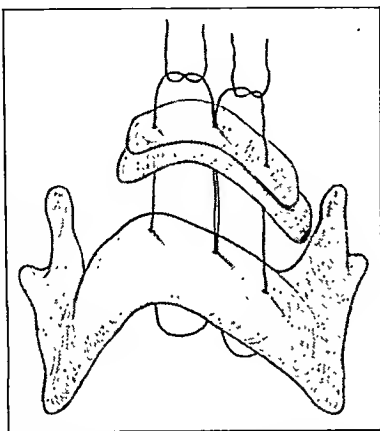


Fig. 2 (see figure 1).—Catgut sutures, inserted through the holes in the jaw, and the overlying cartilage implants, securely anchor the grafts to the mandible.



Fig. 3.—a, Retruded mandible of a girl aged 16 years; this deformity, which had been present for ten years, was secondary to an osteomyelitis of the right ascending ramus of the mandible; b, two pieces of costal cartilage were used to reconstruct the chin, but the lower lip is still retracted by its mucosal attachment to the lower jaw; c, lower lip has been brought forward by a prosthetic appliance inserted in a skin-lined pocket made between the lower lip and the alveolar process.

dary. The primary factors produce an arrest in growth of the mandible or disturb its continuity or conformation. Such factors are osteomyelitis, temporomandibular ankylosis, unreduced fractures of the lower jaw, particularly bilateral subcondylar fractures, and birth injuries. Probably the most serious factor is ankylosis,

which greatly interferes with the function of the jaws and consequently produces an extreme degree of deformity and facial disharmony. The secondary etiologic factors relate to malocclusion which is a complication of the original deformity. As has been stated previously, malposition of the teeth for a period of years always accentuates the primary deformity of the mandible.

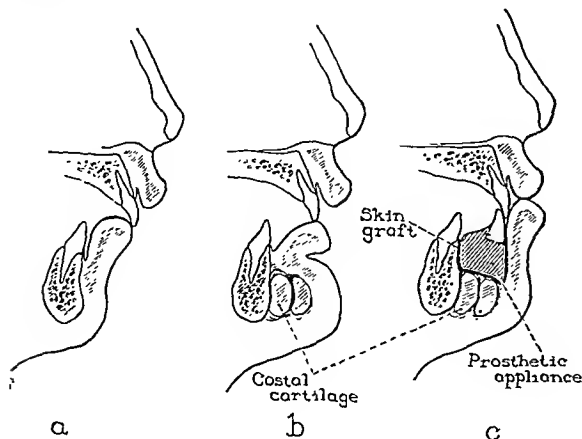


Fig. 4.—Median line section of face of patient shown in figure 3. *a*, preoperative appearance of retruded chin; *b*, two pieces of costal cartilage build out the chin, but the lower lip is still retracted by its mucosal attachment to the lower jaw; *c*, normal contour of lower lip produced by a prosthetic appliance.

The third group includes receding chins in which the teeth are in normal or rather accurate occlusion. Such defects occur rather infrequently and usually are of a congenital nature. An occasional one, however, is the result of malocclusion in which the teeth have been restored to normal articulation by orthodontic measures but in which some residual recession of the chin persists.

OBJECTIVE MANIFESTATIONS

Retruded mandibles vary so greatly in character that it is possible to present only those objective manifesta-

tions which are generally encountered. Mandibular retrusion may be a unilateral or bilateral deformity, more frequently the former. In all such defects of the lower jaw there is some degree of bony hypoplasia; often there is an actual loss of bone with much distortion of the anatomic landmarks of the mandible. Malocclusion is invariably present.

Bilateral retrusion is characterized by posterior displacement of the entire lower jaw. Underdevelopment and recession of the

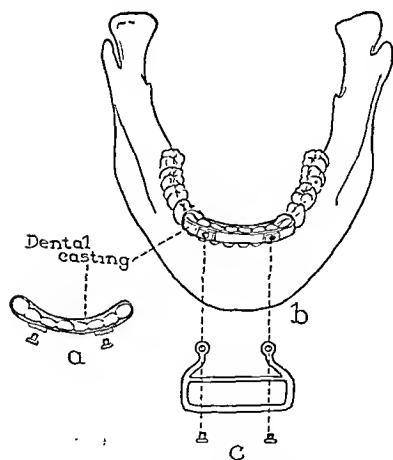


Fig. 5.—Appliance for fixation of a skin graft used in lining a pocket between the lower lip and alveolar process for reception of a prosthetic appliance: *a*, cast silver dental splint as seen from above; *b*, casting cemented to lower anterior teeth; *c*, wire frame for holding dental modeling compound around which the skin graft is wrapped; two small screws which anchor the wire frame to the casting also are shown.

symphysis accentuate the deformity. Occasionally the lower teeth possess a forward inclination, but those whose long axis is more or less vertical often come in contact with the mucous membrane of the anterior por-

tion of the palate. When the defect is associated with mouth breathing, the upper anterior teeth are usually tilted forward, owing to a shortening and lack of development of the upper lip.

In unilateral retrusion the involved half of the mandible is diminished in length. As a result there is a flattening of the unaffected side of the face with an inclination of the chin to the affected side.

In all cases of mandibular retrusion, the most conspicuous feature of the deformity is the retraction or recession of the chin. This may be associated with shortening of the upper lip, asymmetry of the nasolabial sulci and other marks of facial disharmony. It is such distortion of features which primarily concerns the plastic surgeon.

TREATMENT

In the treatment of retruded chin and deformities of the mandible, many procedures have been advocated. They may be grouped as follows: (1) various types of osteotomy through the horizontal or ascending ramus to lengthen or advance the mandible; (2) osteotomy through the horizontal ramus associated with the use of bone grafts to lengthen the mandible; (3) cartilage implants inserted behind the head of the condyles for

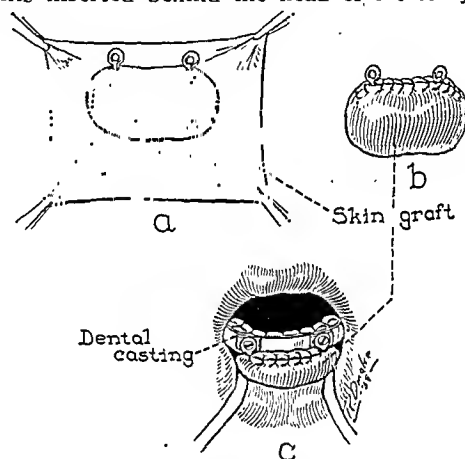


Fig. 6.—Application of skin graft to dental appliance: *a*, after packing dental modeling compound around the wire frame (fig. 5 *c*) and into the intra-oral pocket so as to form a stent for the cavity, a Thiersch skin graft from the inner aspect of the thigh is wrapped about this stent which previously has been coated with rubber cement or mastisol; *b*, the skin graft is sutured over the upper surface of the stent; *c*, the stent covered with the skin graft is inserted into the intra-oral pocket; this method gives perfect fixation of the graft during the healing period.

advancement of the mandible; (4) cartilage, bone, ivory and celluloid implants for building up the chin to normal contour; (5) prosthetic appliances requiring the use of intra-oral skin grafts for restoration of normal chin contour, and (6) orthodontic methods.

In the presence of this rather imposing number of recommended procedures, a consideration of the treatment of retruded mandibles may be somewhat confusing. Moreover, a critical but impartial comment of the value and shortcomings of these various methods is difficult to present, since it is not possible for one to have had personal experience with all of these therapeutic technics; no doubt, each procedure is advantageous in some cases. It is certain, however, that no single method is adaptable for the treatment of every patient with a retruded mandible.

Since a retruded chin or mandible is a deformity of progressive severity during the developmental period of the jaws, the sooner that treatment can be instituted in these cases, the more satisfactory will be the ultimate results. This, perhaps, is the most important consideration in the management of these lower jaw defects.

The majority of retruded mandibles essentially due to malocclusion can be entirely corrected by orthodontia if the disturbed dental articulation is observed early in the life of the patient. In fact, it is best if orthodontic measures can be set in operation before the permanent

period of fixation; for these individuals a pleasing cosmetic correction can be secured in a comparatively short time by plastic methods.

In cases in which a receding chin is unassociated with malocclusion, treatment by a plastic operation is the simplest and most effective means of repair.

In the majority of cases of mandibular retrusion in which plastic methods are indicated for correction of the visible deformity, a cartilage or bone implant may be employed for reconstruction of the chin. Some surgeons recommend ivory or celluloid for this purpose because such material can be cut with great precision and ease previous to the operation. However, we do not favor the use of foreign materials. If only a small graft is required, either costal cartilage or bone obtained from the crest of the ilium may be utilized with equally satisfactory results; but, when the degree of retrusion is pronounced, necessitating an implant of large dimensions, cartilage is the tissue of choice, since two or three pieces may be sutured one over the other to furnish an adequate bulk of material. The use of more than one thickness of bone, of course, is out of the question. We prefer fixed cartilage in which its elasticity has been diminished and its tendency to warp thus lessened.

Before attempting reconstruction of the chin with either a bone or a cartilage implant, it is advisable to obtain a plaster impression of the patient's face. From this impression one may prepare a wax model on which the chin can be built to proper proportions in modeling clay. Such representation of the portion of the chin to be constructed gives one a clear conception of the

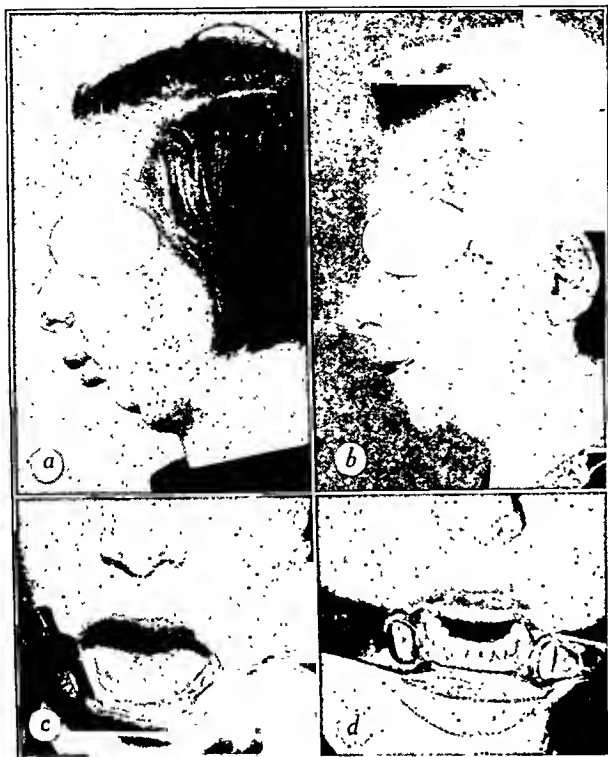


Fig. 7.—*a*, retruded mandible of a girl aged 15 years; this deformity had been present for five years and was secondary to an ankylosis of indeterminate cause involving the left temporomandibular articulation; *b*, following an arthroplasty, the deformity of the chin was corrected by the combined use of a cartilage implant over the symphysis and by an intra-oral prosthetic appliance; *c*, pocket prepared for reception of prosthesis, situated between the lower lip and alveolar process and lined with a Thiersch skin graft; *d*, prosthesis in position.

teeth erupt. If these defects are left untreated until adult life is reached, we believe that plastic procedures for establishing the normal contour of the chin are indicated. Adult patients with malocclusion whose lower teeth are displaced distally usually have but little functional disability as far as mastication is concerned, but we prefer not to increase this inefficiency of the jaws by the use of osteotomy to lengthen or advance the mandible merely for cosmetic purposes.

Retruding mandibles resulting primarily from an arrested bony growth are seldom rectified by orthodontic methods alone. However, in properly selected cases, very satisfactory results can be obtained by an osteotomy to lengthen or advance the mandible and, if feasible, may be followed by orthodontic measures to create normal dental occlusion. In cases of severe unilateral mandibular retrusion an osteotomy is contraindicated because, with the advancement of the anterior fragment, the condyle of the unaffected side is markedly rotated, which interferes with the normal movements of the joint. We have seen a few retruded mandibles which were so greatly underdeveloped and displaced so far posteriorly that no type of osteotomy could begin to lengthen or advance the mental portion sufficiently; in such cases, plastic procedures alone can be employed to correct the defect. It has been our experience that many patients with a retruded mandible decline to undergo an osteotomy because of the long but necessary



Fig. 8.—*a*, retruded mandible of a man aged 25; this deformity had been present for fourteen years and was the result of an osteomyelitis of the body of the mandible; *b*, owing to the marked degree of mandibular retrusion, the deformity could be corrected neither by an osteotomy nor by a cartilage implant over the symphysis; instead, a prosthesis was inserted in a skin-lined pocket between the lower lip and the alveolar process; *c*, artificial teeth of prosthetic appliance occlude with the upper anterior teeth, hide the patient's malposed lower teeth and establish a semblance of normal dental occlusion.

amount of bone or cartilage that will be required. Moreover, it permits of the preparation of lead patterns, which furnish the surgeon with specific measurements when cutting and shaping the implant.

Our patients who require a bone or cartilage graft for reconstruction of a retruded chin are given a general anesthetic. We administer nitrous oxide and ether through an intratracheal tube. The necessary amount of bone or cartilage is procured first and wrapped in a saline sponge until needed. If the defect of the chin amounts to nothing more than a slight recession and is not associated with malocclusion of the teeth, only a small skin incision in the submental region is necessary. Working through this incision with blunt forceps or dissecting scissors, a pocket is created over the symphysis for the reception of the graft. Meticulous care is taken to ligate all bleeding vessels, as hemostasis is most essential in maintaining the viability of the implant. The graft is next cut to the desired contour. In shaping cartilage, we employ only a scalpel; bone, however, requires the use of ronguers, files and bone-cutting forceps. These minor defects of the chin can be corrected nicely by a small graft which needs no fixation to the mandible. The implant is inserted over the sym-

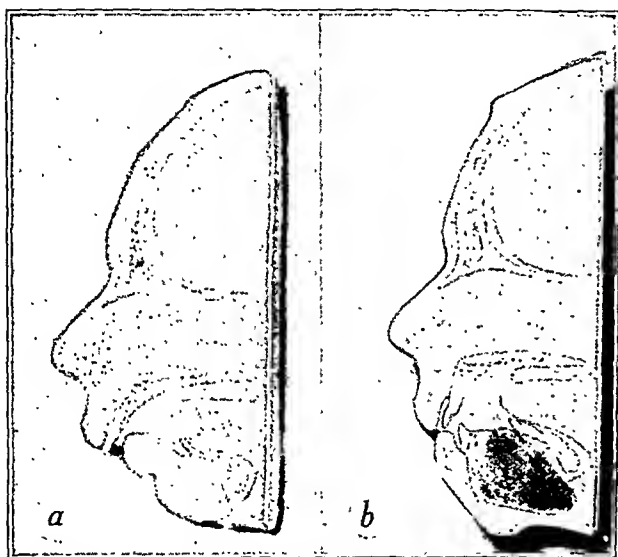


Fig. 9.—Median line section of face of the patient shown in figure 8; a, preoperative appearance of retruded lower jaw; b, normal contour of chin produced by prosthesis inserted into a skin-lined pocket between the lower lip and the jaw.

physis through the skin incision and is immobilized in correct position by external pressure.

In cases of definite mandibular retrusion associated with dental malocclusion, a transverse skin incision is made through both submaxillary regions about 2 cm. below the lower border of the mandible. By undermining the soft tissues the anterior portion of the lower jaw is exposed. Careful dissection is required to prevent nicking through the oral mucous membrane, which would be disastrous. In the majority of these cases a comparatively large graft is required; this necessitates the use of cartilage. Often, one thickness of cartilage is insufficient to correct the deformity fully. If such should be the case, two or three pieces may be sutured together with fine catgut. While hemostasis is being established in the wound, the cartilage is cut to the desired shape and adapted over the symphysis. Grafts of any appreciable size require internal as well as external fixation. Consequently, with a motor driven drill, three holes about 1 cm. apart are made through the cartilage and underlying bone (fig. 1). Through these holes is inserted a piece of heavy chromic catgut which, when tied, securely anchors the graft in position (fig. 2).

The soft tissues then are sutured over the implant and the edges of the skin are approximated with sutures of fine black silk. To prevent the collection of serum in the tissue spaces, a Penrose drain is inserted into the wound. External pressure is applied as a final step in the operation.

Since most patients with a retruded chin have considerable distal displacement of the lower teeth in relation to the upper dental arch, an acceptable cosmetic result is not effected by the mere use of a cartilage implant over the chin. On the contrary, the deformity is actually accentuated by the insertion of the graft because the lower lip accordingly is drawn back tensely by its mucosal attachment to the gum tissue over the lower anterior teeth (figs. 3 and 4). This retraction of the lower lip can be corrected by incising the mucosal attachment and inserting a prosthetic appliance between the lip and alveolar process in a skin-lined pocket (figs. 3 and 4). This appliance possesses artificial teeth which articulate with the upper anterior teeth, hide the malposed lower teeth and establish a semblance to natural dental occlusion.

To free the lower lip from its attachment to the lower alveolar process, sharp dissection is employed and an incision is made through the mucous membrane of the labio-alveolar sulcus from one bicuspid region to the other. This incision is carried down between the alveolar process and lower lip to the cartilage implant, care being taken not to expose the graft. The result of this procedure is the creation of a pocket which must be lined with skin for the reception of the artificial appliance.

The problem in skin grafting such a cavity is the difficulty in obtaining absolute fixation of the part during the healing period. Needless to say, immobilization is one important factor in successful skin grafting. We have developed the following technic for maintaining perfect fixation; without exception, this method has given excellent results: As a preliminary measure, a silver cast dental splint, which is cemented to the lower teeth, is required (fig. 5). On the anterior aspect of this casting are two threaded holes into which steel screws may be turned (fig. 5). A wire frame is also constructed which can be securely fastened by the screws to the casting (fig. 5). Following the preparation of the pocket between the lower lip and alveolar process, the wire frame is fixed to the casting and adjusted so as to lie in the center of the wound. It is then removed and is coated with a thin layer of dental modeling compound which has been melted in a flame. This compound, softened in this manner, will adhere perfectly to the frame, whereas a compound softened in hot water will not. After reattachment of the compound-covered frame to the casting, a cake of modeling compound is softened in hot water and packed down around the frame into the pocket. When hard, the compound and frame are securely united and together form a stent that is perfectly adapted to all the irregularities of the pocket. On removal from the mouth, the stent is coated with rubber cement or mastisol (a solution of mastic in benzene). A thin Thiersch skin graft (from the inner surface of the thigh), which is cut preliminary to the intra-oral operation, is wrapped about the stent and sutured along its upper surface (fig. 6). The stent covered with the skin graft is then inserted into the pocket and screwed to the dental casting (fig. 6). Adhesive plaster applied externally firmly fixes the lower lip to the stent, which is immovable. With the elapse of ten days, the stent may be removed and the pocket will be found to be lined perfectly with skin

(fig. 7). Inserted into this cavity is the prosthetic appliance which is attached by clasps to the lower teeth (fig. 7). The use of such an artificial apparatus combined with a cartilage implant insures a pleasing esthetic result in many cases of retruded chin (figs. 3 and 7).

We previously have mentioned patients whose mandibles are so greatly underdeveloped and displaced so far posteriorly that no type of osteotomy could begin to advance the mental portion of the jaw sufficiently (figs. 8 and 9). Even a cartilage implant would be useless in such a case, as it would be impossible to insert a large enough graft to bring the chin forward in a normal position. We believe that the simplest method of correcting the external deformity of such a severely retracted mandible is to use an intra-oral prosthetic appliance (figs. 8 and 9). The pocket to be lined with skin is extended down around the lower border of the mandible; this aids in the retention of the appliance. While lining this cavity with skin is similar to that already described, the prosthetic apparatus must be hollowed out to reduce its weight. For a few days after the appliance is inserted, the lower lip, which is stretched and tense, has a tendency to contract downward; to counteract this retraction, adhesive tape must be used to hold the lower lip in the desired position. As a matter of fact, about six months is required for the muscles of the lower lip to develop sufficiently to maintain the lower lip in a natural manner. By this method a very marked retrusion of the mandible can be effectively corrected in a short time; at least, the facial contour can be satisfactorily restored to normal proportions (figs. 8 and 9).

HEARING AIDS—TUBE OR CARBON?

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Electric hearing aids¹ today have become instruments of considerable importance and of many different designs. They may be for large audiences in theaters, schools, churches and auditoriums or for small groups in homes and offices. All of these use line current and are generally stationary. However, most instruments now are designed for individual use and only for the use of one individual, are of "vest pocket" size, use battery current and are wearable. For the last two years, these wearable instruments have been built with small ("peanut" size) radio tubes and crystal microphones. This is the most radical change in hearing aids since 1932.

The development and refinement of the electric hearing aid and the modern radio receiving set both began in 1922. The former has followed the latter quite closely in many ways and has been to a considerable degree dependent on it. Alexander Graham Bell's original electric hearing aid was the only instrument then (1922) available. It had to fit all cases, even though its air conduction receiver, carbon transmitter and battery had remained essentially unchanged for almost exactly fifty years.

During the next ten years (1922 to 1932) progress consisted largely of the development of refinements. Molded ear tips and smaller receivers were among the

first improvements to be made. The ear tip held the receiver in the external auditory canal, obviating the necessity of strapping it on the head or holding it up against the ear with the hand. Amplifiers or boosters soon were added to the transmitter. Both of these, as well as the receivers, could peak amplification at the frequencies indicated by the audiogram, and mechanical filtering could level off the objectionable peaks inherent to carbon, thus converting a disadvantage into the decided advantage of selective amplification. Batteries were enlarged to three dry cells with greatly prolonged life.

In 1932 Hugo Lieber introduced his bone receiver. This carried sound vibrations around middle ears, whose oval windows were blocked, directly into the inner ear. The bones of the skull thus took the place of the air in the canal, to the enormous benefit of the otosclerotic whose auditory nerves were still even fairly good. Soon in place of the Bell type single air conduction instrument (fig. 1) for all cases, hundreds of carbon aids (fig. 2) of different acoustic characteristics were available for both bone and air conduction that could be fitted, within limits, by prescription from otologists' audiograms by the selection of proper transmitters, amplifiers, receivers and batteries to correct almost any hearing loss that was correctable. And otologists had learned from their audiograms that no two hearing losses were exactly identical.

Meanwhile in 1922 radio ceased being just "wireless," mostly for ships at sea, and came into American homes and offices as "receiving sets." About 100,000 sets and 2,000,000 tubes were sold that year. By 1939 these sales had increased to 9,000,000 sets and 100,000,000 tubes. In sixteen years radio had become a half-billion dollar business, just one of the industries that the vacuum, or thermionic, tube had made possible.

The family tree² of these tubes and the place that tubes for hearing aids occupy on it are extremely interesting. All of this modern development followed the pioneer research of Edison (effect, 1883), Fleming (valve, 1905), De Forest (audion, 1906) and many others, notably Henry, Maxwell, Herts and Marconi. "Peanuts" came into quantity production for general use in 1920, three element tubes for loud speakers in 1925 and small peanut tubes for hearing aids in 1932.

At first these tubes, still quite large, could be used only in desk sets, but, as the smaller type "peanuts" were developed and lighter equipment became available, wearable tube aids were possible. These eliminated the time honored carbon transmitter of Alexander Graham Bell.

By 1938 "peanuts" had become so small and so economical in current consumption they could be used in wearable aids (fig. 3) and could be energized by A and B batteries no larger and no heavier than those for carbons. Now, after nearly two years' experience, the question "hearing aids—tube or carbon?" is both pertinent and important. Although the mass of evidence necessary for well founded scientific judgment is not yet available, some comparisons and conclusions are possible.

Comparisons may be briefly summarized as follows:

1. Tubes amplify up to 6,000 or maybe to 8,000 cycles, carbons only to 3,300 or thereabouts. The former should correct perceptive hearing loss and restore the high tones of music and the overtones of both speech and music, on which the timbre

Dr. Hayden died, July 10.
Read before the Chicago Laryngological and Otological Society, April 1, 1940.

1. Stevens, S. S., and Davis, Hallowell: *Hearing*, New York, John Wiley & Sons, Inc., 1938, p. 59.

2. *Electronics*, New York, McGraw-Hill Book Company, October 1938.

of each so largely depends. Carbon aids cannot do this. That is the reason why music does not sound well over even the new telephone receivers (carbon).

2. Tubes give "straight line" amplification instead of the "distorted" amplification of carbons.

3. Tubes are more complex in construction, as yet less dependable in performance and more difficult and costly to buy, service and keep up.

4. Short circuits that will ignite are more apt to occur and burn clothing or person with 20 to 60 volt batteries (tube aids) than with 3 to 6 volt batteries (carbon aids).

5. Failure of the tube aid is sudden, unpredictable and without warning. A factory or a special service station is necessary for repair. The carbon aid deterioration is gradual and repairable usually by simple cleaning and introduction of new carbon without the necessity of attention from a factory or special service station.

In the cases in which nerve function is good, tube aids give brilliant results; but these are the very cases in which carbon aids were also accepted well. However, patients with severe perceptive loss above 3,000 cycles—the point at which the pain threshold falls so rapidly—often experience discomfort and frequently

On the other hand, those with conductive loss do not experience this difficulty and accept tubes well, but frequently not any better than carbons except in frequencies above 3,300 cycles, which is of course extremely important for music and speech overtones.

Extraneous noise, unavoidable in carbons, is much less in the tube aids. To a person with good ears this would seem at first thought to be a great advantage, but hearing aids are designed for ears that do not hear well. Consequently this noise is inaudible to them and therefore not objectionable.

Both tube aids, which are new, and carbon aids, which are old, are being constantly improved. The entire satisfaction that many who are hard of hearing derive from the use of tube aids is well known and unquestioned.

One of the "big four" manufacturers of hearing aids, however, makes only carbon aids. That the development in carbon receivers is constant is evidenced by the fact that the new telephone receivers—from 500 to 2,500 cycles instead of from 500 to 1,000 (the old type)—are a great improvement; and the fact that there

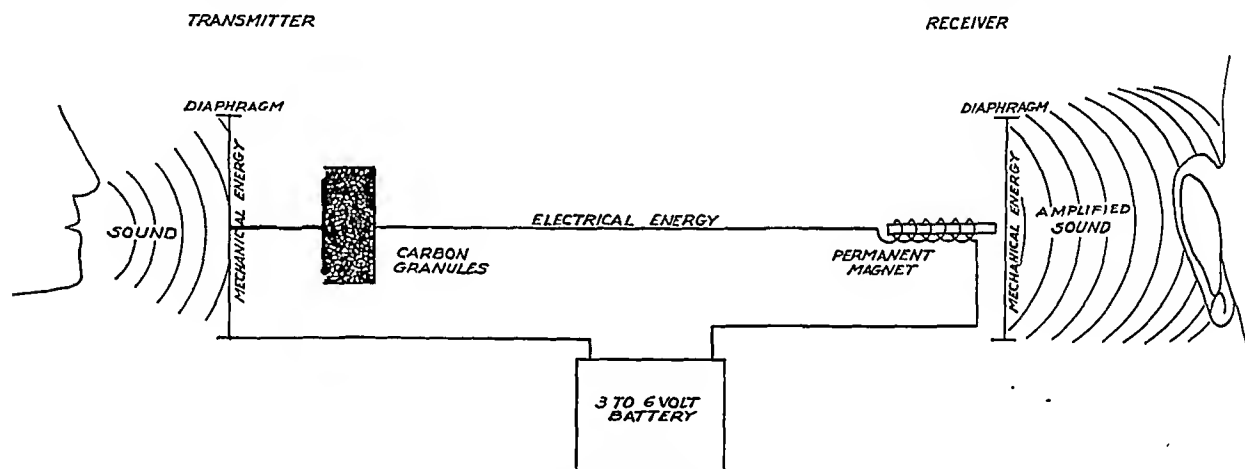


Fig. 1.—Original Bell type carbon hearing aid (schematic diagram of circuit, from Lectures on Hearing Aids and Audiometers, by Howard A. Carter). This consisted of a simple transmitter, battery and receiver. Its function was to amplify speech by the application of electrical energy. For fifty years this was the only hearing aid available for all types of deafness.

do not obtain satisfactory improvement in hearing. These are the patients who physicists reasoned should be helped most by the straight line, high frequency amplification of tubes.

The reason for the failure of the tube aid to help these persons with perceptive loss is probably the position and diminished size of their auditory area.³ This is displaced to the left on the audiogram. Low frequencies are retained, but the high tones to the right are lost. It is a generally recognized principle in fitting hearing aids that the response curve of the instrument must be kept within the auditory area. When this is not done and the amplification of the "straight line" crosses the upper limit of the auditory area, which is the pain threshold, discomfort occurs that rapidly becomes actual pain, if the maximum intensity of the instrument is turned on. In other words, the auditory areas of many of these persons with perceptive loss simply cannot accept the amplification the tubes can produce at the high frequencies.

3. Stevens and Davis define this as the area lying between the thresholds of hearing and feeling. The latter varies all the way from a tickle through an itch to what Kekesy describes as a painful burning similar to that produced by severely rubbing the skin but felt deep down inside the ear. Usually this is referred to as the threshold of pain.

are 400,000,000 telephones in the world means that a tremendous amount of research will continue to be done in carbon equipment. Whether the ultimate in hearing aids will be a descendant of Edison's electric light bulb and De Forest's radio tube or a very greatly refined development of Alexander Graham Bell's carbon hearing aid coming essentially as an outgrowth of his telephone, time alone can tell. Carbon instruments have been and still are the model T of hearing aids. From these data, from clinical experience and from contact with otologists, physicists, hearing aid manufacturers and patients the following conclusions seem warranted:

CONCLUSIONS

1. At present both tube and carbon aids have definite advantages and disadvantages. Both are being improved constantly.

2. Indications for each must be formulated from the experience of otologists, physicists and manufacturers, with the final decision made by the patient.

3. Tube aids give more brilliant hearing improvement in conduction loss when nerve function is good. In severe perceptive loss, results are often disappointing.

4. Purchase from a firm that manufactures both carbon and tube aids, for air as well as bone conduc-

tion, allows choice between the two and makes exchange of one for the other easier.

5. Since tube aids are much more complex instruments, the need for an impartial evaluating agency such as the Council on Physical Therapy of the American Medical Association, to set and maintain requirements

7. Tube aids are as yet more expensive to manufacture, buy, keep up and service.

8. Whether tube aids will supplant the carbon type of hearing aid or vice versa, or whether each will eventually occupy its own definite field, with the actual improvements that are being made in construction by

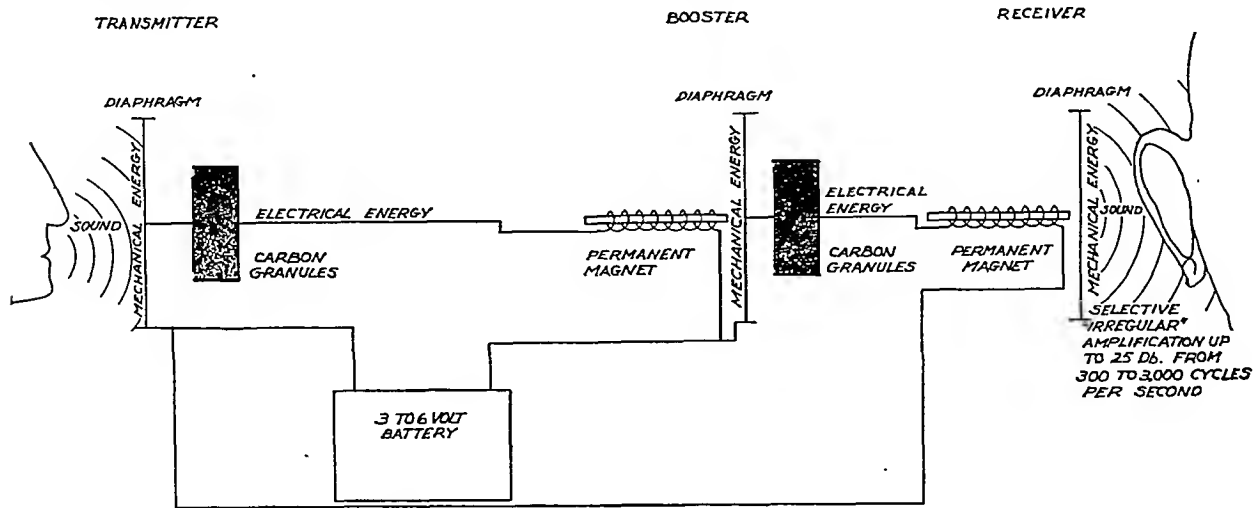


Fig. 2.—A modern carbon hearing aid (schematic diagram of circuit, from Lectures on Hearing Aids and Audiometers, by Howard A. Carter). This is a simple sturdy dependable instrument with a larger battery and an amplifier or booster that operates on low voltage (from 3 to 6 volts). It has much more amplification (going up to 25 or 30 decibels) than the original, with a frequency ranging from 300 to 3,000 cycles per second. Amplification is "distorted" but selective and capable of being peaked into one to three areas of hearing loss. Some extraneous noise is unavoidable. The only service required is occasional cleaning and replacement of carbon, all of which can be done by any service station. The aids adapt themselves equally well to both bone and air fittings. Batteries give ample warning of failure. Short circuits are not likely to burn. Expense of purchase and upkeep is less than for a tube aid.

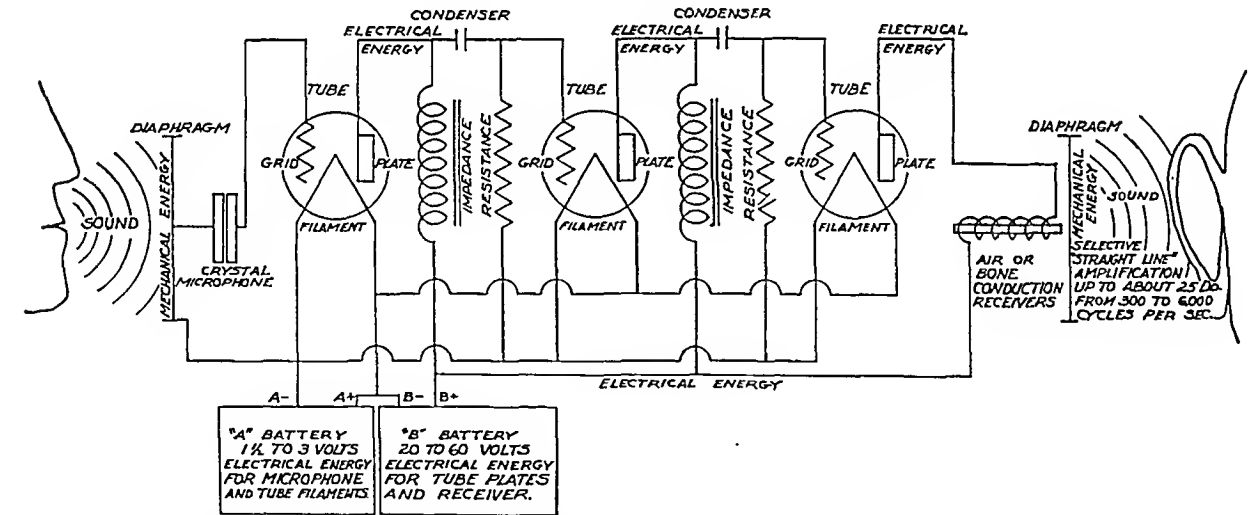


Fig. 3.—Tube hearing aid (schematic diagram of circuit, from Lectures on Hearing Aids and Audiometers, by Howard A. Carter). This is necessarily a complex and fragile instrument compared with the carbon type. It is free from carbon noise but has tube and battery noise. (Tube noise is a ringing sound from jars and quick movement, or a mushy sound if tube filament or grid wires are off. Rubbing the case by clothing or hand amplifies the rustling sound.) It gives uniform, undistorted amplification generally spoken of as "straight line." Its tubes (from two to four), choke, transformer, condensers, resistors, switches, jacks and soldered connections (from four to six for each tube) all make it so. The chokes and transformers have to be wound with such fine wire (half the diameter of the human hair) that they are extremely delicate and consequently sensitive to falls, strains and moisture. The high voltage (from 20 to 60 volts) current can burn if short circuited. Complete and sudden failure of performance without warning occurs when batteries or parts give out, the life of the latter being variable and unpredictable. It must be sent to the factory or a specified station for service. It is more expensive to buy as well as to keep up.

for acceptance of standards of construction and performance as well as of sales ethics and advertising, is even more necessary with the advent of tube aids. Financial rating of the manufacturers is very important.

6. Although the lure of radio tubes is great, patients should not discard carbon for tube aids without careful investigation.

manufacturers and in the prescription of hearing aids by otologists, good results are now obtained by the vast majority of patients properly fitted with a well made hearing aid.

9. Even better instruments and better hearing seem to be on the way.

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SOLITARY CECAL DIVERTICULITIS

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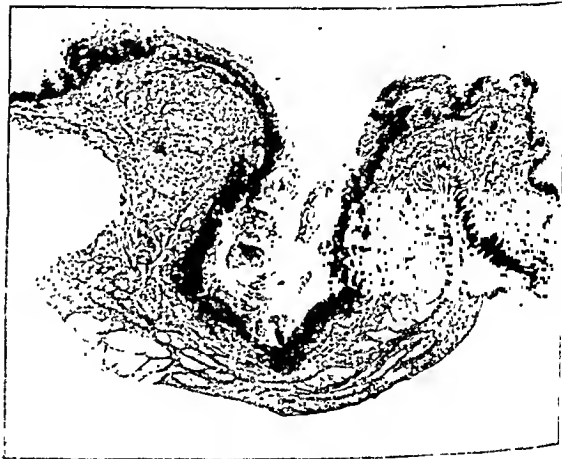
The general surgeon is probably called on to operate in the right lower quadrant of the abdomen more frequently than in any other region and here preponderantly for inflammatory lesions of the vermiform appendix. It is my purpose in this paper to call attention to a condition closely resembling appendicitis, a condition which is seldom considered in the differential diagnosis and one which is scarcely mentioned in any of the standard textbooks of surgery. In discussing a series of 118 cases of diverticulitis of the colon, Judd and Pollock¹ made no mention of cecal diverticulitis simulating appendicitis. Solitary cecal diverticulitis should not be confused with multiple diverticulitis, which may involve the cecum and ascending colon—examples of this condition having occurred from time to time in the surgical service of Johns Hopkins Hospital. Instances of solitary cecal diverticulitis have been reported in the literature from time to time and during the past year three cases have been recognized at this hospital. These cases together with two others of less recent date, as well as fifteen cases taken from a review of the literature, form the factual data for this communication.

REPORT OF CASES

CASE 1.—An Italian housewife aged 50 was admitted April 27, 1934, complaining of pain in the right lower quadrant of the abdomen. Because of language difficulties an accurate history was not obtained. She had never been operated on. For about one month she had had fairly constant pain, always localized to the right lower quadrant and never associated with nausea or vomiting. Her appetite had remained good and she had had neither constipation nor urinary symptoms. Physical examination showed definite tenderness and slight muscle spasm throughout the right lower quadrant of the abdomen. The temperature was 99.2 F., the pulse rate 88, the respiratory rate 20 and the blood pressure 106 systolic, 66 diastolic. The urine was normal. The white blood cell count was 9,100. The Wassermann reaction was negative. A diagnosis of appendical abscess was made and immediate operation done (Dr. Eldridge Campbell) under nitrous oxide-ether anesthesia through a McBurney incision. The appendix was normal and lay free without any adhesions. An inflammatory mass was found lying just lateral and posterior to the cecum and had evidently originated in a small inflamed diverticulum at the base of the cecum. The diverticulum, containing a small fecalith, was excised and the resulting aperture closed with a purse-string of silk. The appendix was removed and the wound drained and closed with catgut. The patient's convalescence was smooth and she was discharged ambulatory and afebrile on the twentieth day. A barium sulfate enema done before her discharge showed a normal colon without any evidence of diverticula. She was well when seen two years later. Microscopic examination showed a normal appendix and an inflamed diverticulum consisting of mucosa, submucosa and edematous subperitoneal fibrous tissue. No muscularis was identified.

CASE 2.—An American housewife aged 28, admitted June 27, 1939, complained of abdominal pain. Her past history was essentially negative. A week before admission she had been seen in several of the outpatient departments because of obesity and infectious arthritis in the left ankle. At that time some tenderness and slight muscle spasm had been elicited over McBurney's point. In an attempt to find a focus of infection for her arthritis, roentgenograms of the upper gastrointestinal tract and of the gallbladder by the Graham-Cole test were done, but these yielded negative results. About eighteen hours

before admission she began having dull pain throughout the entire lower part of the abdomen. She lost her appetite and became nauseated but did not vomit. During the succeeding hours these pains, which she described as sharp and aching but not cramplike, gradually localized in the right lower quadrant. The patient was obese and was in considerable distress although not acutely ill. There was diffuse muscle spasm and slight tenderness throughout the right lower quadrant of the abdomen with maximal tenderness at McBurney's point. Vaginal and rectal examinations showed slight tenderness high on the right side. The temperature was 99.6 F., the pulse rate 84, the respiratory rate 24 and the blood pressure 104 systolic, 72 diastolic. The hemoglobin content was 88 per cent and the white blood cell count 9,800. The urine was normal. The flocculation test gave negative results. A diagnosis of acute appendicitis was made and immediate operation done (A. J.) under avertin with amylene hydrate and nitrous oxide-ether anesthesia. A McBurney incision was made through the thick panniculus. There was no free fluid within the abdomen and the appendix was perfectly normal. Beneath the cecum a firm mass the size of a small hen's egg was readily palpable. It was delivered and found to be a large, acutely inflamed diverticulum lying between the two folds of the mesentery. Because of the size of the lesion and its proximity to the blood supply of the cecum, inversion or excision seemed inadvisable. Accord-



Section through the specimen taken in case 2; slightly reduced from a photomicrograph with a magnification of $3\frac{1}{2}$ diameters.

ingly a right midrectus incision was made and the cecum, including the lesion, appendix and ascending colon, resected. Because of the disparity in caliber of the divided ends of the ileum and transverse colon, an end to side anastomosis was done with interrupted silk sutures. The abdomen was closed with silk, no drainage being used. A transfusion of 500 cc. of citrated blood was given. Convalescence was marked by abdominal distention for which duodenal drainage gave some relief. On the fourth day she commenced having normal bowel movements and thereafter her convalescence was smooth. She was discharged ambulatory and afebrile on the eighteenth day. When seen two months later she was in excellent health. Pathologic examination showed a cecal diverticulum measuring 4 by 4 by 25 cm. All layers of the intestine were present, although the muscularis was considerably thinned. The entire structure, especially at its tip, was acutely inflamed, and there was considerable inflammation in the surrounding fatty tissue, as shown in the accompanying illustration.

CASE 3.—A Negro chauffeur aged 47, admitted July 10, 1939, complained of abdominal pain. His past history was essentially negative. Three days before admission he had commenced experiencing cramplike pains in the right lower quadrant of the abdomen. These had been associated with marked anorexia and had been severe enough to prevent his sleeping. His bowels had moved regularly until two days before admission, when he took a dose of solution of magnesium citrate which produced several loose stools but gave no relief from the pain. The

From the Department of Surgery, Johns Hopkins University School of Medicine and Hospital.

1. Judd, E. S., and Pollock, L. W.: Diverticulitis of the Colon, *Ann. Surg.* 50: 425 (Sept.) 1924.

patient was muscular; he was uncomfortable but not acutely ill. The abdominal muscles showed no definite spasm, but deep palpation about 2 inches medially to the right anterior superior iliac spine elicited constant tenderness. There was no rebound tenderness. The temperature was 99.8 F., pulse rate 78, respiratory rate 24 and blood pressure 130 systolic, 85 diastolic. The urine was normal. The flocculation test gave negative results. The hemoglobin content was 16 Gm. The white blood cell count was 8,100. A diagnosis of acute appendicitis was made and immediate operation done under avertin with amylene hydrate and nitrous oxide anesthesia through a McBurney incision. The peritoneal cavity contained a small amount of clear, slightly blood tinged fluid. The appendix was in a retroperitoneal position, mobilized, found to be normal and then removed. A small hard mass about the size of an olive was then located on the lateral aspect of the cecum about 2 inches above the appendical stump. The surrounding fat was markedly indurated and reddened. The overlying fat was incised and an acutely inflamed diverticulum about 1 cm. in diameter exposed. A part of it was gangrenous; no fecalith was felt. It was easily inverted through two purse-strings of silk and the abdominal wound closed without drainage. The convalescence was smooth except for a superficial wound infection from which *Bacillus coli* was cultured. He was discharged ambulatory and afebrile on July 26. A week later the wound was entirely healed. Since then the patient has been quite asymptomatic.

CASE 4.—A white woman aged 48, a housewife, admitted May 23, 1939, complained of pain in the right lower quadrant of the abdomen. At the age of 24 she had had several attacks of pain in the right lower quadrant of the abdomen associated with nausea and well localized tenderness. These attacks usually lasted two or three days, gradually subsiding. Two years later she had a similar attack and was admitted to the gynecologic service of this hospital, where an appendectomy was done. The appendix was described as "short and thick and relatively free from adhesions." The cecum was inspected and no abnormalities were noted. A pathologic diagnosis of "chronic appendicitis" was made. She had no further attacks and was quite well until the middle of March 1939, when she experienced severe cramp-like pain in the abdomen for five days. This finally subsided after she took a large dose of magnesium sulfate. Six days before admission she commenced having similar pain, this time in the right lower quadrant of the abdomen. Physical examination showed a well healed McBurney scar on the abdomen. Extending from the level of the upper end of the scar and descending into the pelvis on the right side was a firm, moderately tender mass of rounded contour. It seemed to be slightly larger than the examiner's fist and to lie within the abdominal cavity. Vaginal examination failed to demonstrate any connection between the mass and the pelvic genitalia. The temperature was 99 F., pulse rate 84, respiratory rate 20 and blood pressure 160 systolic, 100 diastolic. The hemoglobin content was 96 per cent. The white blood cell count was 8,250. The urine was normal. The flocculation test gave negative results. X-ray films of the abdomen, the Graham-Cole test, intravenous pyelograms and barium sulfate enema all gave negative results. A preoperative diagnosis of abdominal abscess of undetermined origin was made and operation carried out on June 2 (Dr. Edward Stafford) under nitrous oxide-ether anesthesia through a low right rectus incision. On the anterior surface of the cecum just at its junction with the ileum lay an inflammatory mass well walled off by omentum. The attachments of the omentum were divided and the whole mass removed from the cecum by sharp dissection. This revealed a small hole in the under side of the cecum at some distance from the usual site for the base of the appendix. The opening, which was perfectly flush with the cecal wall, was closed with two layers of catgut sutures. A drain was placed down to the cecum and the wound closed with catgut and stay sutures. The patient's convalescence was smooth and she was discharged ambulatory and afebrile on the fourteenth day. The wound was entirely healed one month after operation and the patient was quite well three months later. Microscopic examination of the tissue removed showed subacute and chronic inflammation.

In the foregoing case it seems highly probable that the inflammatory mass originated from a perforated diverticulum, because the appendix had been cleanly removed eleven years previously and because the point of perforation in the cecum lay some distance from the usual site of the appendical base and to one side of the longitudinal bands of the colon. Nevertheless, one cannot be certain of the etiology. Table 1² summarizes the points of interest in fifteen cases of solitary cecal diverticulitis—the total gathered from a search of the literature.³

CASE 5.—A married woman aged 36, a garment worker, admitted May 27, 1937, complained of abdominal pain of five days' duration. Her general health in the past had been good. Following the onset of generalized abdominal pain she had taken a saline cathartic. This had produced several fluid stools and the pain had localized in the right iliac fossa. At no time had she vomited. The temperature was 100.8 F. (rectal), the pulse rate 100, the respiratory rate 24 and the blood pressure 130 systolic, 70 diastolic. The urine was normal. The white blood cell count was 19,000. Low in the right lower quadrant was an exquisitely tender mass about the size of a hen's egg. The entire abdomen was tender, and rebound tenderness was referred to the right lower quadrant. Vaginal examination gave negative results. A diagnosis of appendical abscess was made and immediate operation done (Dr. Paul Kunkel) under nitrous oxide-ether anesthesia. The cecum presented through a McBurney incision and along its lateral wall and closely adherent to it lay a firm mass resembling an acutely inflamed appendix. "It was exactly like an inflamed appendix curled upon itself save that it was not as long as an appendix and had a much broader base." The mass was resected and its stump inverted through a purse-string suture. The rest of the cecum was then delivered and a normal appendix found on its medial side. This too was amputated and its stump inverted through a purse-string. A normal gallbladder containing a solitary stone was palpated and left undisturbed. The wound was closed with catgut, no drainage being used. It healed nicely and the patient was discharged ambulatory and afebrile on the seventh day. She has had no recurrence of symptoms, but when last seen, thirty months after operation, complained of menorrhagia, probably due to a chronic cervicitis. Unfortunately there was no pathologic study made of either the diverticulum or the appendix.

COMMENT

In the group of cases collected from the literature and tabulated herewith, the operative and pathologic observations are of some interest. French's⁴ first patient had occasional attacks of abdominal pain for one year and had lost some weight but experienced no acute symptoms. The only finding at operation was a solitary cecal diverticulum containing a hard fecalith but showing no evidence of active inflammation. Dislodgment of the fecalith and inversion of the diverticulum, however, resulted in complete cure. Such a case might more properly be classified as one of diverticulosis. Thomsen's⁵ third patient gave a long history of pain in the right lower quadrant and had no acute symptom, and histologic examination of the excised diverticulum showed several small tuberculous ulcers at its junction

2. Because of lack of space table 1 has been omitted in *THE JOURNAL*; the complete article appears in the author's reprints.

3. Jackson, W. R.: Diverticulitis of the Cecum, *New York M. J.* 106: 838 (Nov. 3) 1917. Moschowitz, A. V.: Acute Gangrenous Perforated Diverticulitis of the Cecum, *Ann. Surg.* 67: 624, 1918. Cooke, A. B.: When Appendicitis Is Not Appendicitis: A Case of Diverticulitis of the Cecum, *J. A. M. A.* 78: 578 (Feb. 25) 1922. Pereira, Harold: Diverticulitis of the Cecum, *Brit. M. J.* 1: 279 (Feb. 12) 1927. Leonardo, R. A.: Primary Solitary Diverticulitis of Cecum, *Ann. Surg.* 91: 540 (April) 1930. Stetten, De Witt: Ileocecal Resection for Acute Diverticulitis of Solitary Diverticulum of Ascending Colon, *Ann. Surg.* 104: 478 (Sept.) 1936. Visconti, J. A.: Diverticulitis of Ascending Colon Simulating Acute Appendicitis, *Am. J. Surg.* 32: 376 (May) 1936.

4. French, R. W.: Diverticulitis of the Cecum, with Report of Three Cases, *Boston M. & S. J.* 189: 307 (Aug. 30) 1923.

5. Thomsen, H.: Solitaire cecaldivertikler, *Hospitaltid.* 78: 45 (Jan. 8) 1935.

with the cecum. He gave no information as to the condition of the rest of the intestinal tract nor any report as to the end result. In two instances, the case of Potier⁶ and that of Obenour,⁷ acute inflammation of the appendix and of a diverticulum was found. In both cases the diverticulum opened into the cecum at some distance from the appendix, but sufficient details of existing relationships are not available for one to be certain at which point the process was primary. In Shier's⁸ case the diverticulum was situated in the ascending colon, yet the whole picture is so typical that it is included here.

It is customary to classify diverticula in two groups: (1) true, when all the normal layers of the intestine—mucosa, submucosa, muscularis, and serosa—are present, and (2) false, when the muscularis is absent. Such a classification is based on the assumption that false diverticula represent outpouchings through weak points in the muscularis. Of the cases here reviewed, sufficiently detailed pathologic descriptions are provided in nine, six of them being classified as true diverticula and three of them as false. This distinction should not be considered as arbitrary, for unless serial sections are made through the entire specimen a thinned-out layer of muscularis may be missed entirely. Conversely, in a

TABLE 2.—Age Distribution

Age in Years	Number of Cases
0 to 9.....	0
10 to 19.....	1
20 to 29.....	4
30 to 39.....	2
40 to 49.....	3
50 to 59.....	7
60 to 69.....	2

false diverticulum the section may be eccentric, passing through a layer of muscularis, and an erroneous diagnosis may be made.

Inflammation of a solitary cecal diverticulum may apparently occur at any age, the ages in the cases here reviewed ranging from 10 to 64 years, seven of the patients, or 36.8 per cent, being under the age of 40. This is in sharp contradistinction to the age incidence of multiple diverticulitis, for Brown⁹ at the Mayo Clinic found that of 191 cases of colonic diverticulitis treated surgically only 5.2 per cent occurred under 40 years of age—a proportion with which other reports are in substantial agreement. Since appendicitis too occurs at any age, it would seem that the age factor is no aid in the diagnosis of solitary cecal diverticulitis. Moreover it would appear that the condition is seldom associated with the multiple or widespread form of the disease. Of my five patients, two had completely negative barium studies of the colon, the third underwent a negative exploration of the rest of the colon, while the fourth and fifth have not returned for a follow-up barium enema study. Of the cases summarized from the literature, two more were shown by complete exploration and barium enema to have the process confined to the cecum.

Most of the diverticula contained one or more fecaliths; they were present in at least thirteen of the nineteen cases, or 68.4 per cent, and probably play a considerable role in the etiology of the inflammation. While it is rare for perforation of an inflamed cecal diverticulum to result in peritonitis, it is common for perforation to result in abscess formation, as it did in eight of the aforementioned cases. Widespread peritonitis is a rare sequela, perhaps because of preëxisting adhesions to the omentum and to the parietes. The resulting abscesses are usually thick walled and fairly discrete and not infrequently lie adjacent to the mesentery or even between its two leaves. The abscesses are so intimately attached to the cecum, so tumefied and so frequently associated with enlarged mesenteric lymph nodes that it is not uncommon for the surgeon to mistake the condition for malignant tumor of the cecum. Occasionally the true nature of the condition is not made clear until the specimen is opened or sectioned. Others of the resulting abscesses are so completely walled off that it is possible to dissect them quite free from the cecum with a minimum of contamination.

One might expect x-ray studies by means of barium sulfate enemas to be of value in a differential diagnosis involving the condition. Not only is a barium sulfate enema contraindicated in the acute stage of the disease because of possible further dissemination of infection but it is frequently ineffectual in demonstrating the presence of a diverticulum which is plugged by inspissated feces or filled by an actual fecalith. It is a common observation among roentgenologists that of all the diverticula present in the multiple form of the disease only a small proportion are usually demonstrated by a single barium sulfate enema.

As for the proper operative procedure to employ, one should use the simplest compatible with eradication of the condition. A small uncomplicated diverticulum may be inverted through a purse-string. A larger diverticulum may require excision before inversion. Large inflamed diverticula lying close to the ileocecal valve or between the leaves of the mesentery so as to jeopardize the cecal blood supply require extensive resection. For lesions in this region the practice in this clinic is to resect a few inches of terminal ileum, cecum and ascending colon, completing the procedure, if possible, by an end to end anastomosis between ileum and transverse colon at a point at which the colon has a nearly complete peritoneal coat. Discrete abscesses and inflammatory masses may be dissected free when possible, although such a procedure risks spreading of infection. Adherent abscesses and those involving the parietes are better drained than removed.

In the entire series not a single fecal fistula has resulted. Since in a considerable proportion of cases the process is limited to a single diverticulum, the condition should be treated with the end in view of permanently curing the condition rather than palliating it, as of necessity is the case in multiple diverticulitis. Additional evidence of the solitary nature of the condition is afforded by the fact that patients properly treated have remained perfectly well without any gastrointestinal symptoms for long periods.

One may agree heartily with Stetten and Abeloff:¹⁰ "The condition . . . is rather prevalent and should always be borne in mind in questions of differential

6. Potier, F.: Diverticulité et appendicite, Bull. et mém. Soc. anat. de Paris 37: 29, 1912.
7. Obenour, S. W.: Gangrenous Diverticulum Associated with Suppurative Appendicitis, Ohio State M. J. 34: 175 (Feb.) 1938.
8. Shier, R. V. B.: Acute Diverticulitis of the Ascending Colon, Canad. M. A. J. 39: 264 (Sept.) 1938.
9. Brown, P. W.: The Treatment and Prognosis of Diverticulitis of the Colon, Am. J. Surg. 46: 162 (Oct.) 1939.

10. Stetten, De Witt, and Abeloff, A. J.: Observations on the Clinical Picture and Therapy of Diverticulitis of the Colon, J. Mt. Sinai 110: 4: 781 (March-April) 1938.

diagnosis of an acute abdomen. It should always be looked for at operation if other findings do not satisfactorily explain the clinical picture, and the surgeon should always be prepared to deal appropriately with the condition."

SUMMARY

1. Solitary cecal diverticulitis is an unusual condition which closely simulates appendicitis clinically.

2. It should always be considered in the differential diagnosis of pain in the lower part of the abdomen and should be searched for at operation if the other conditions do not explain the clinical picture.

3. It may occur at any age and is prone to progress to perforation and abscess formation, but if properly treated it should, in contradistinction to multiple diverticulitis, result in a permanent cure.

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SYPHILIS OF THE BONES IN INFANCY

SOME POSSIBLE ERRORS IN THE ROENTGEN DIAGNOSIS

WILLIAM A. EVANS JR., M.D.

DETROIT

The recent stimulation of interest in the detection and treatment of syphilis warrants comment on some of the special problems involved. One of these is the diagnosis of congenital syphilis. Antepartum examinations and the treatment of syphilitic women during pregnancy have prevented many cases of syphilis in the offspring but have made the diagnosis of congenital syphilis even more difficult. In most cases the diagnosis is either finally confirmed or excluded by the serologic studies or by the roentgen examination of the long bones. An early decision is important, for prompt treatment is necessary to prevent the occurrence of permanently damaging lesions; on the other hand, unnecessary treatment is particularly troublesome and harmful to the health and even life of a child.

A positive serologic reaction alone is of doubtful validity, for it is known that the property of producing a positive test may be transferred from the maternal blood to the fetal blood without the fetus being syphilitic (Filde's law). Christie¹ has recently confirmed this and has shown that some help is offered by the quantitative measurement of the complement fixing antibodies. If these are present in a nonsyphilitic child at birth their concentration in the serum will rapidly diminish and disappear in about three weeks. If the child is syphilitic there will be no decrease or only a temporary decrease in the titer, and a rise in the titer in a period of from four to six weeks will indicate a definite syphilitic infection. A negative serologic test in the newborn child is also inconclusive, for many children who eventually show evidence of syphilis have a negative serologic test at birth. This circumstance was observed in 37 per cent of the syphilitic children studied by Cooke and Jeans² and in 33 per cent by Ingraham.³ Ingraham

recommends the dark field examination of scrapings of the umbilical vein for making an early diagnosis in doubtful cases.

The roentgen examination of the long bones attained importance particularly through the studies of Pendergrass and Bromer,⁴ Vogt⁵ and McLean,⁶ and there is no doubt that characteristic osseous lesions are found in a very high percentage of cases of fully developed syphilis. The diagnosis in the less obvious cases is more difficult, however, and both positive and negative errors may be made. At the Children's Hospital of Michigan, routine x-ray studies of the long bones of premature infants and of infants in whom syphilis is suspected have been carried out for a number of years, and some of these problems have come to our attention.

FALSELY NEGATIVE ROENTGEN EXAMINATION

A child may show no osseous lesions or other evidence of syphilis at birth and after several weeks or months definite manifestations of congenital syphilis may develop. In the material studied by Ingraham⁷ this was a common circumstance, being observed in one half of the cases. His observations indicated that from four to six weeks is required after the infection of the fetus for osseous lesions to appear. If this occurs early, i. e. in the fifth month of pregnancy, the lesions will be fully developed at birth. If, on the other hand, the infection does not occur until shortly before birth, osseous lesions will not become manifest until the second or third month of life. We have recently observed three cases of this type:

CASE 1.—B. C., an illegitimate white girl, was born three weeks prematurely of a syphilitic primiparous woman who had received intravenous and intramuscular antisiphilitic treatment for two months prior to delivery. She was admitted to the

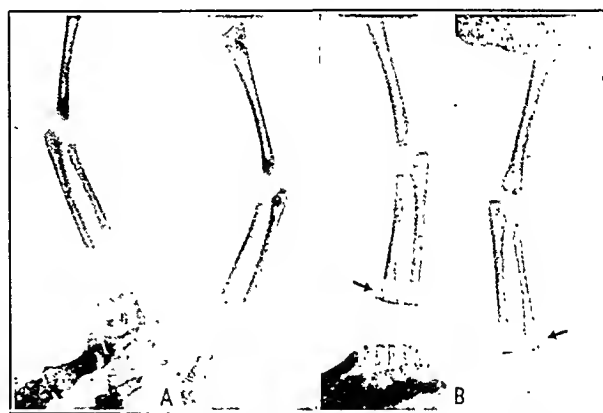


Fig. 1 (case 3).—The first examination (A), made at 7 days of age, revealed no characteristic syphilitic lesions. The second study (B), two months later, showed a destructive syphilitic osteochondritis at the lower ends of both radii.

Children's Hospital at 1 month of age because of twitchings of the extremities. The physical examination was negative, but there was a strongly positive blood Kahn test and the spinal fluid contained 300 white cells per cubic millimeter, although

4. Pendergrass, E. P., and Bromer, R. S.: Congenital Bone Syphilis, *Am. J. Roentgenol.* 22:1 (July) 1929.

5. Vogt, E. C.: The Value of the Roentgenography in the Diagnosis of Congenital Syphilis, *Am. J. Roentgenol.* 26:96 (July) 1931.

6. McLean, Stafford: Correlation of Roentgenographic and Pathologic Aspects of Congenital Osseous Syphilis with Particular Reference to First Months of Life, *Am. J. Dis. Child.* 41:363 (Feb.) 1931; Correlation of the Roentgenologic Picture with the Gross and Microscopic Examination of Pathologic Material in Congenital Osseous Syphilis, *ibid.* 41:607 (March) 1931.

7. Ingraham, N. R., Jr.: The Lag Phase in Early Congenital Osseous Syphilis, *Am. J. M. Sc.* 191:819 (June) 1936.

From the Department of Roentgenology of the Children's Hospital of Michigan.

1. Christie, A. U.: Diagnosis of Syphilis in Newborn Infants: Use of Quantitative Wassermann Tests, *Am. J. Dis. Child.* 55:979 (May) 1938.

2. Cooke and Jeans, cited by Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1927, p. 1013.

3. Ingraham, N. R.: The Diagnosis of Infantile Congenital Syphilis During the Period of Doubt, *Am. J. Syph. & Neurol.* 19:547 (Oct.) 1935.

the spinal fluid Kahn test was negative. The roentgen study of the long bones revealed no abnormality. No definite diagnosis was made at this time; but on the second admission one month later, for a recurrence of symptoms, the liver and spleen were found enlarged, both blood and spinal fluid Kahn tests were positive, and well developed syphilitic lesions were observed in the long bones by x-rays. The child improved under specific therapy and there was regression of the osseous lesions.

CASE 2.—W. G. was a 7 month premature Negro child born of a 23 year old woman suspected of having syphilis but untreated. At the time of birth the cord blood Wassermann test was positive, and for this reason four injections of bismarsen were administered. The infant was admitted to the Children's Hospital at the age of 33 days with some edema of the legs. Over a period of three months the infant's blood Kline test was negative four times and positive twice and one Kahn test was negative. The maternal blood Kline and Kahn tests were both positive twice and negative twice. Clinically the child presented a feeding problem, with dietary anemia and edema. The first roentgen study of the long bones was negative, except for some submetaphysal demineralization which we regarded as the result of the nutritional disturbance. Questionable syphilitic changes were seen in the long bones at the study six weeks later, but a positive diagnosis could not be made until more definite changes were observed after another four weeks, at about 3 months of age.

CASE 3.—M. K. was born prematurely at 7 months of an apparently healthy Negro woman. The hospital admission occurred at 17 days of age because of bronchopneumonia. No changes were observed in the bones at that time (fig. 1), and two blood Kline tests were negative. Both parents, however, exhibited positive Kline reactions of the blood. Two months later a second roentgen study of the bones revealed typical syphilitic changes, and the infant died two days later.

These three cases illustrate some of the difficulties in making an early diagnosis of congenital syphilis

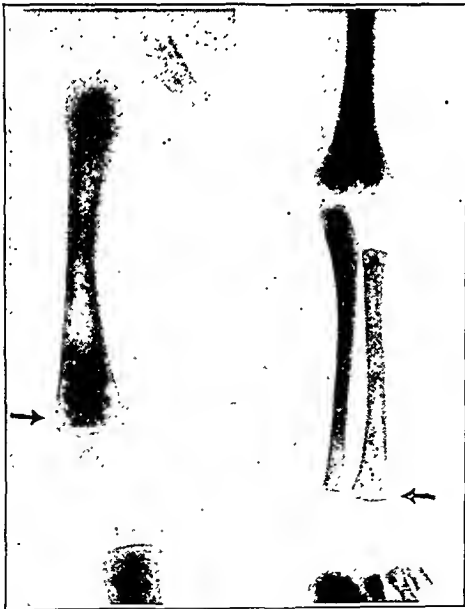


Fig. 2 (case 4).—Well developed submetaphysal rarefaction with increased density of the metaphysal line in an infant of 1 week with hemolytic icterus. No evidence of syphilis had appeared in an observation period of five months.

when the evidence is conflicting or inconclusive. Often the observations must be continued through a period of doubt lasting two or three months before a positive diagnosis can be made, and then it may be too late for effective treatment.

FALSELY POSITIVE ROENTGEN EXAMINATION

The hazards of making a false diagnosis of syphilis, illustrated by the following group of cases, arise from an improper interpretation of changes occurring in the metaphysal areas and of periosteal shadows and defects in the diaphysis.



Fig. 3 (case 5).—Periosteal proliferation was observed at the lower medial aspect of the right tibia of a 1 week old infant examined because of failure to use the right leg and evidence of pain. No evidence of syphilis appeared and the periosteal reaction subsided as shown by the last study, made at 7 months of age. This is probably an instance of subperiosteal fracture sustained at breech delivery.

Bands of rarefaction or condensation are frequently seen at the ends of the diaphyses, especially in premature infants and those presenting nutritional disturbances. These changes cannot be regarded as specific. Although some observers⁸ have offered such evidence as indicative of syphilis, their nonspecific character has been recently emphasized by Christie⁹ and Caffey.¹⁰

CASE 4.—J. D. was admitted to the hospital at the age of 1 week with anemia and jaundice and a feeding problem. The liver and spleen were enlarged and the red blood cell count was 3,500,000. X-ray studies of the long bones (fig. 2) revealed a striking band of rarefaction in the submetaphysal areas. The Kahn test was negative. On a second admission at 5 months of age for a respiratory infection the blood and spinal fluid Kline tests were negative and there were no clinical signs of syphilis.

Periosteal shadows vary from the very fine white line parallel to the shafts of the long bones, most commonly the femurs, to a very heavy onion-like cloaking of the bone which may double the diameter of the shaft. In the newborn and young infants such a finding has in the past been considered¹¹ pathognomonic of syphilis, but this is certainly not true. Causes of these periosteal shadows are found not only in syphilis but also in subperiosteal fractures occurring at delivery,¹² in rickets.

8. Parmelee, A. H., and Halpern, L. J.: Diagnosis of Congenital Syphilis, *J. A. M. A.* 105: 563 (Aug. 24) 1935.
9. Christie, A. U.: The Value of Roentgenographic Examination in the Diagnosis of Syphilis in Newborn Infants, *J. Pediat.* 15: 230 (Aug.) 1939.
10. Caffey, John: Syphilis of the Skeleton in Early Infancy, *Am. J. Roentgenol.* 42: 637 (Nov.) 1939.
11. Chiari, Ottokar: Ueber periostale Reaktionen bei nicht luetischen Kindern im ersten Trimenon, *Acta paediat.* 22: 436, 1938.
12. Snedecor, S. T.; Knapp, R. E., and Wilson, H. B.: Traumatic Ossifying Periostitis of Newborn, *Surg., Gynec. & Obst.* 61: 385 (Sept.) 1935.

in tuberculosis and other forms of osteomyelitis¹⁰ and in a considerable group of cases in which the cause is obscure. In the latter group may be instances of hypertrophic pulmonary osteo-arthritis associated with chronic pulmonary or cardiac disease as suggested by Meier.¹³ It also seems likely that irregularities in periosteal new bone formation causing a laminated appearance of the cortex may occur as the result of nonspecific growth disturbances in the same manner as the irregularities of enchondral ossification which lead to transverse striations at the ends of the diaphyses.

CASE 5.—D. F., a private patient of Dr. J. J. Pollack, was born of a primiparous woman by a breech delivery. At 1 week of age there was an apparent paralysis of the right leg. Some redness and swelling were noted over the tibia, but there were no signs of a generalized infection or of any abnormality within the chest. Blood Kahn tests were negative on both parents and the child. X-ray examinations (fig. 3) revealed a definite periosteal shadow at the lower end of the right tibia. Further studies over a period of seven months showed an uneventful growth of the child, and there was gradual disappearance of the periosteal shadow. Although no fracture line was demonstrable, we believe this to be an example of a subperiosteal fracture sustained at birth and manifested by pain and refusal to use the leg and by the callus which appeared at the fracture site.

Rickets is most often discovered in the last half of the first year of life and is recognizable by very characteristic changes at the ends of the diaphyses of the

long bones. In addition to the disturbance in calcification of the metaphysial areas, however, there is a failure of calcification of new bone laid down by the periosteum, and this leads to an irregularity in the cortex of the shaft and the appearance of periosteal separation, or "cloaking," which closely resembles an inflammatory periostitis. True rickets is practically unknown in the newborn and is uncommon in the second or third month of life. At this age the roentgen manifestations are often atypical and in our experience may be confined to the shafts of the long bones with very inconspicuous changes in

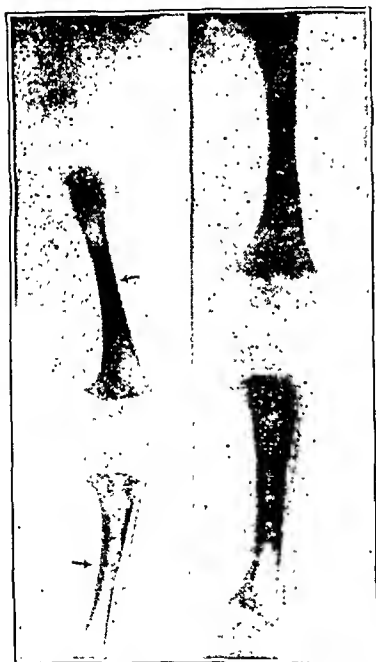


Fig. 4 (case 7).—A Negro child born of syphilitic parents was examined at 2 months of age as a syphilitic suspect, although serologic tests were negative. Periosteal shadows were noted about both femoral and tibial shafts. No other signs of syphilis appeared, and the study at 1 year showed typical changes of rickets. The periosteal shadows observed at the first examination were probably rachitic in nature.

the metaphysial areas. In such instances a diagnosis of syphilitic periostitis may be entertained. McLean⁶ has emphasized that rachitic periosteal cloaking may

closely simulate the periostitis of syphilis and reports an instance in a 3 week old Negro child in which the diagnosis was made at autopsy.

CASE 6.—R. Z., one of twins born Jan. 31, 1939, was admitted to the Children's Hospital May 5 with a skin rash, fever



Fig. 5 (case 8).—A 1 year old child whose mother was suspected of having syphilis. The study showed widespread lesions involving the skull, mandible, small bones of the hands and feet, and periosteal proliferation about the long bones. A diagnosis of syphilis could not be established, and a positive tuberculin test, the clinical behavior of the lesions and biopsy indicated the tuberculous character of the process.

and jaundice. There was progressive bronchopneumonia, and death occurred May 20. Serologic tests on the patient and both parents were negative for syphilis. X-ray studies of the long bones revealed a striking degree of widespread periosteal reaction most marked in the ribs, femurs and tibias. The epiphyses were not yet demonstrable, and the only change in the metaphyses was a slight lippling at the corners. Postmortem examination showed bronchopneumonia, hepatitis and rickets, the last mentioned diagnosis being confirmed by microscopic study. The patient's twin brother, who was hospitalized at the same time, exhibited similar bone changes and made a satisfactory recovery.

CASE 7.—M. E., a Negro child, was born June 7, 1938. Both parents had had antisyphilitic therapy and the mother was treated during the pregnancy. A diagnosis of syphilis had been made on a sister 1 year old and she was under treatment. The patient had been breast fed but had received no cod liver oil. No physical abnormalities were noted, but because of the family history a roentgen study was made of the long bones Aug. 9, 1938 (fig. 4), which showed periosteal shadows. The Kline and Kahn serologic tests were negative and the patient was not treated for syphilis. The child was again seen June 21, 1939, and typical x-ray evidence of advanced rickets was obtained. In view of the florid rickets and the failure of syphilis to develop, we have concluded that the periosteal shadows observed at 2 months of age were in all probability rachitic in nature.

Inflammatory lesions other than syphilis which may involve the bones in infancy must also be given consideration. In our experience osteomyelitis is rare at this age, but Caffey¹⁰ has reported cases of gonococcal and staphylococcal osteomyelitis with accompanying periostitis in infancy. Tuberculous involvement of shafts of the long bones is rarely seen, especially in

13. Meier, A.: Periostitis hyperplastica bei einem 3 Monate alten Frühgeborenen, Arch. f. Kinderh. 109: 223, 1936.

infancy, but we have recently encountered one such case which offered a problem in differential diagnosis:

CASE 8.—J. W. was an illegitimate white child born by normal full term delivery. The 17 year old mother was said to have acquired and been cured of syphilis at 10 years of age. At the age of 10 months the patient was observed to have an enlargement of the left foot and left middle finger. On the admission to the outpatient clinic two months later x-ray studies revealed extensive osseous and periosteal lesions (fig. 5). In spite of repeated negative Kahn reactions in both mother and child and a strongly positive tuberculin test, the diagnosis of syphilis was entertained and specific treatment carried out with acetarsone for eight weeks. This was without demonstrable effect on the lesions, and hospitalization was advised for further study. It was learned that there had been cervical adenitis at the age of 6 months following pertussis with drainage from a fistulous tract for four months. The child appeared well nourished and happy. There was only slight anemia (hemoglobin 10.8 Gm. per hundred cubic centimeters), and during the hospital stay of five weeks there was rarely a significant temperature elevation. Attempts to obtain material by aspiration of the left first metatarsophalangeal joint were not successful. Further x-ray studies revealed cystlike lesions in the skull and mandible; there was no definite involvement of the lungs or mediastinum. Dec. 1, 1939, biopsy was carried out on the lesion in the right hand; microscopic examination of the caseous material which was removed showed a cellular structure having every appearance of tuberculous granulation tissue.

The first case of so-called cystic tuberculosis in childhood was reported by Schwentker in 1931. His patient was also 1 year of age and gave a stronger suspicion of syphilis but did not show the expected improvement under antisyphilitic treatment. This case and one reported by Vastine and Bacon¹⁴ are very similar to ours. The lesions are indolent in character, are usually discovered accidentally and produce little local or systemic reaction. Only eleven cases of cystic tuberculosis of the bones in children were collected by Law and Perham¹⁵ in 1938, and five of the patients were under 2 years of age, which testifies to the rarity of this condition.

CONCLUSIONS

1. The diagnosis of congenital syphilis has become more difficult and the manifestations of the disease are more obscure since antepartum examinations and the treatment of syphilis during pregnancy have become common.

2. Osseous lesions may not appear in a syphilitic infant until several weeks after birth, and the early x-ray studies may therefore be negative.

3. Striations and bands of rarefaction at the ends of the diaphyses and periosteal shadows or a laminated appearance of the cortex may be the result of a non-specific disturbance of nutrition and growth and cannot, without other evidence, be regarded as indicative of syphilis.

4. In young infants rickets may be manifest by prominent periosteal shadows with minimal changes in the metaphysal areas. Other causes of periosteal shadows are subperiosteal fracture, cardiopulmonary osteo-arthritis and a large group of cases in which the cause is obscure.

5. Tuberculosis and other infections may also produce osteal and periosteal lesions simulating syphilis in infancy.

10 Peterboro at Woodward.

THE EFFECT OF HORMONES ON THE UNDESCENDED TESTIS

AN EXPERIMENTAL AND CLINICAL STUDY

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MAX APPEL, M.D.

AND

MAX FRAENKEL, M.D.

CHICAGO

The subject of undescended testis has been of great interest to one of us (J. S. E.) for over twenty years. In previous publications we have reported our results of operative treatment. Our point of view has changed somewhat and has been broadened by the work of other surgeons in this field and by our own increased experience. In this communication we are concerned chiefly with the newer methods of treatment now in vogue—the attempt to bring undescended testes into their proper position in the scrotum by the use of hormones. Those in which we are interested are the gonadotropic hormones derived from the anterior lobe of the pituitary gland and similarly acting water-soluble substances derived from the urine of pregnant women.

The literature during the past five or six years has been replete with reports of brilliant results by this mode of therapy. Some of the reports are so enthusiastic as to astound one. Here and there appear scattered reports of doubters and the expressed opinion that these substances may be of little or no value in the treatment of instances of true undescended testis and, in fact, may be actually harmful in certain instances when given in larger doses.

Those who have written of the high percentage of successful results do not seem to have been critical of the actual anatomic status of the abnormally situated testis. They apparently have failed to differentiate between the various positions which a retractile testis may occupy from testes in the true undescended positions and from those in ectopic positions.

The recent work of Denis Browne¹ seems to offer a basis of classification which, while not perfect, clarifies the situation considerably and corresponds with our clinical and anatomic conceptions of the problem. Browne divides the positions of the testes into three large categories, under each of which are several sub-heads: first, the normal positions, in which the testis invariably will descend spontaneously to the bottom of the scrotum by the time its growth is complete; second, the undescended positions in which the testis has been arrested in its line of travel from the region of the kidney to the scrotum, at some point from which there will be no spontaneous descent; third, the ectopic positions in which there is a turning aside from the direct line of descent below the external inguinal ring. In general we are in agreement with this classification but feel that a more descriptive term should be used to describe the so-called normal positions, because at least at the time the boys come for medical or surgical care the testis does not occupy its proper position, even if it may do so later without treatment.

From the Urological, Pathological and Metabolic departments of Michael Reese Hospital.

Read before the North Central Branch of the American Urological Association at Indianapolis, Sept. 26, 1939.

Dr. Otto Saphir and Dr. Samuel Soskin gave many helpful suggestions and offered the facilities of their laboratories in order that this work might be done.

1. Browne, Denis: Brit. M. J. 2: 168 (July 23) 1938.

14. Vastine, J. H., and Bacon, E. P.: Osteitis Tuberculosa Multiplex Cystica, *Radiology* 24: 22 (Jan.) 1935.

15. Law, J. L., and Perham, W. S.: Multiple Cystic Tuberculosis of the Bones in Children, *Am. J. Dis. Child.* 56: 831 (Oct.) 1938.

Our interest in the effect of hormones on the undescended testis was first aroused when we operated on a series of thirteen patients who had failed to respond to injections of anterior pituitary-like substance given by their physicians. We had previously operated on 177 patients who had not received hormone therapy and for that reason feel more or less conversant with the usual manifestations in this condition. In all instances the testes of patients who had received the larger dosages of hormone presented a very peculiar appearance and had a markedly reduced consistency. The dividing line between the smaller and the larger dosages for our purpose is approximately 6,000 rat units total dosage. In those patients receiving less than a total of 4,000 rat units the testis at operation did not appear unlike the many undescended testes on which we had operated in patients who had not received endocrine therapy. However, the adhesions present were more numerous and firmer than those in patients who had not received this type of treatment. In those who had received 6,000 rat units and more the testes invariably were smaller than in untreated patients or in patients who had received the smaller dosages. A comparison

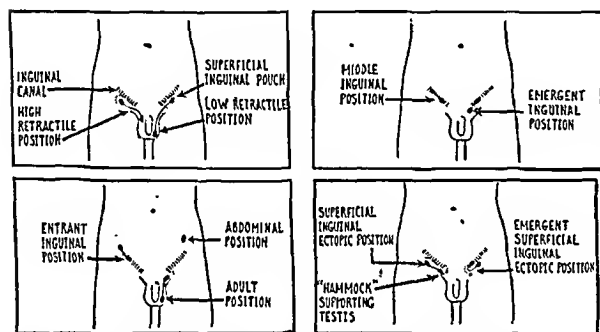


Fig. 1.—Diagram used for recording the position of the testes. It shows by conventionalized design the inguinal canal and the superficial inguinal pouch. The position of the testicle is charted by a black oval at each end of its range of movement, connected by a black line. Taken from Browne's article in the *Lancet*.

seemingly could be made between the amount of hormone given and the period over which it had been used and the diminution in the size of the testis. In one instance observed at our hospital the testis appeared merely as a slight nodule, hardly wider than the spermatic cord. This patient was operated on by Dr. M. L. Parker, and we have his permission to report the case. The surface of all testes which had been subjected to the larger dosage of hormone invariably presented a peculiarly mottled appearance, and they were all definitely reduced in consistency. We have verbal confirmation of identical observations made by Drs. Rolnick, Lieberthal and W. J. Baker. The appearance of these testes was so striking that we concluded that the injections of hormones might have produced these changes, and this was the reason for beginning our experimental work about eighteen months ago. In the meantime there have appeared one or two papers on this subject which present results somewhat similar to our own.

It is interesting to learn the fate of the abnormally situated testis when left untreated before and after puberty. Johnson's² recent paper is enlightening on this question. He observed the spontaneous descent of over

50 per cent of abnormally situated testes in a group of boys. The largest number of cases of spontaneous descent occurred at the age of 12 years, but in many instances the testes descended spontaneously up to and through the age of 17 years. Drake³ insists that in the great majority of cases of cryptorchidism the gonads

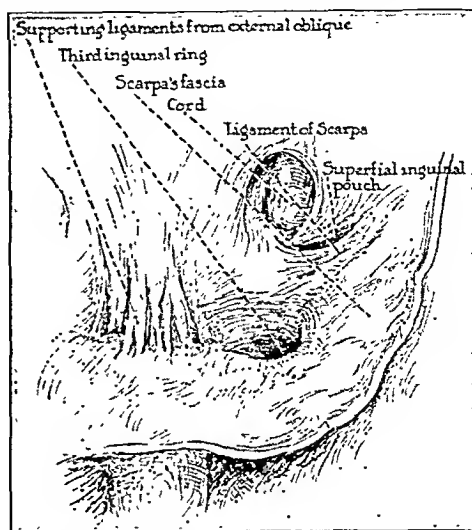


Fig. 2.—The superficial inguinal pouch is well shown in this dissection; it is between Scarpa's triangle or the deep layer of the abdominal fascia and the external oblique muscle; it is filled with very lax areolar tissue and is about the size and shape of the scrotum. From McGregor, A. L.: *Surg., Gynec. & Obst.* 49:292 (Sept.) 1929.

will reach the scrotum at or shortly after puberty. McCahey⁴ found that in testes which were fixed in their abnormal position he was not successful in bringing about complete descent into the scrotum with endocrine therapy. "The maximum effect obtained in these cases was to have the testes descend to the lowest point to which previously it had been possible to move

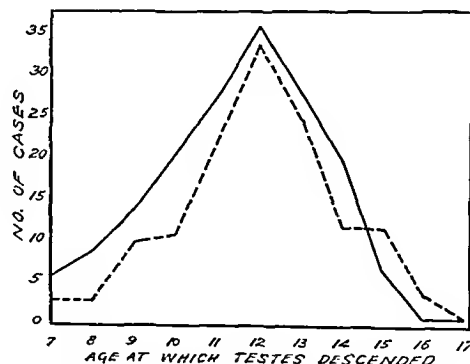


Fig. 3.—These curves are plotted from the results found by W. W. Johnson in his observations of 31,609 boys examined. Of these, 246 had bilateral nondescent, making 492 testes in malposition, and 298 boys with unilateral nondescent, a total of 790 testes in abnormal positions. Of these, 500 descended spontaneously. Note that the curves are quite parallel for bilateral and unilateral malposition. Solid line, bilateral descent; broken line, unilateral descent.

them, and sometimes retraction later occurred." Thompson and Heckel⁵ in their most recent publication say

3. Drake, C. B.: Spontaneous Late Descent of Testis, *J. A. M. A.* 102:759-761 (March 10) 1934.

4. McCahey, J. F.: Gonadotropic Hormone Therapy in Cryptorchidism and Disturbances of Spermatogenesis, *Pennsylvania M. J.* 41:359-363 (Feb.) 1938.

5. Thompson, W. O., and Heckel, N. J.: Undescended Testes: Present Status of Glandular Treatment, *J. A. M. A.* 112:397-403 (Feb. 4) 1939.

2. Johnson, W. W.: Cryptorchidism, *J. A. M. A.* 113:25-27 (July 1) 1939.

"The effect of the anterior pituitary-like principle from the urine of pregnant women in the treatment of undescended testes appears to be exaggerated. It follows that in the majority of true undescended testes opera-

become increasingly good and series published by Counsellor⁹ and by Walters and Thiessen¹⁰ show that good to excellent results were achieved in from 92 to 93 per cent of patients operated on. Our own statistics show 87 per cent falling in these categories. This high percentage of good results, we are sure, has also been achieved by numerous operators in this country. The proponents of endocrine therapy have failed to recog-

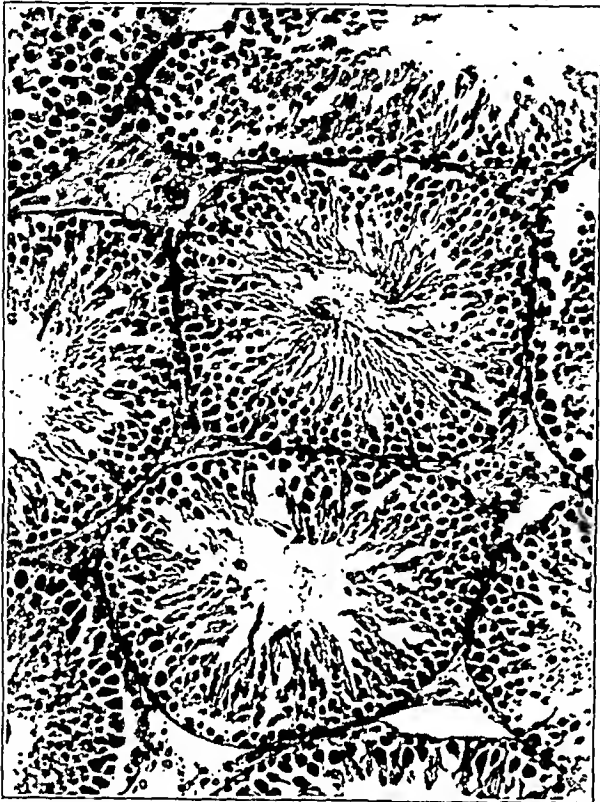


Fig. 4.—Section of normally situated testes from a treated animal. Note the active spermatogenesis in all the tubules. Hematoxylin-eosin stain, $\times 160$.

tive procedure is still necessary because of mechanical factors which prevent descent. It is possible that this material causes descent only of those testes which will descend without treatment about the time of puberty." One could continue citing references from the literature showing a point of view which seems to parallel our own. However, there are relatively few references to the harmful effect of the use of endocrine therapy. Mimpriss,⁶ Cabot,⁷ Cole⁸ and Evans have all observed definite degenerative processes produced by the injection of gonadotropic substance either in man or in the experimental animal. Denis Browne says "I submit that the hormone treatment of undescended testes is dangerous, useless and founded on an anatomic error." Johnson concludes that, "judged in the light of the outcome without therapy, endocrine therapy should be used only as an adjunct to oncoming puberty and in reality is not a necessity." It is interesting to note the solicitous attitude of some authors who, after calling attention to the microscopic changes noted in undescended testes, say that "their observations make one question the advisability of waiting for the spontaneous descent of the testis." They also cite the poor results of operative correction to support their predilection for hormone therapy. The results of operation, however, in competent hands have

TABLE 1.—Weights of Normally Situated and Cryptorchid Testes in Treated and Untreated Animals

Rat No.*	Normally Situated Testes (Weight in Milligrams)	Cryptorchid Testes (Weight in Milligrams)
1.....	1,300	1,120
C 2.....	1,400	720
4.....	1,420	720
C 5.....	1,510	720
6.....	1,490	850
C 7.....	1,750	710
8.....	1,590	300
9.....	1,860	550
10.....	1,780	600
11.....	1,460	720
12.....	1,130	700
C 14.....	1,580	525
15.....	1,670	680
16.....	1,560	770
17.....	1,580	1,190

* O before rat number indicates untreated or control animal.

nize that the danger inherent in the use of larger doses of anterior pituitary-like substance is greater than the delay in waiting for spontaneous descent.

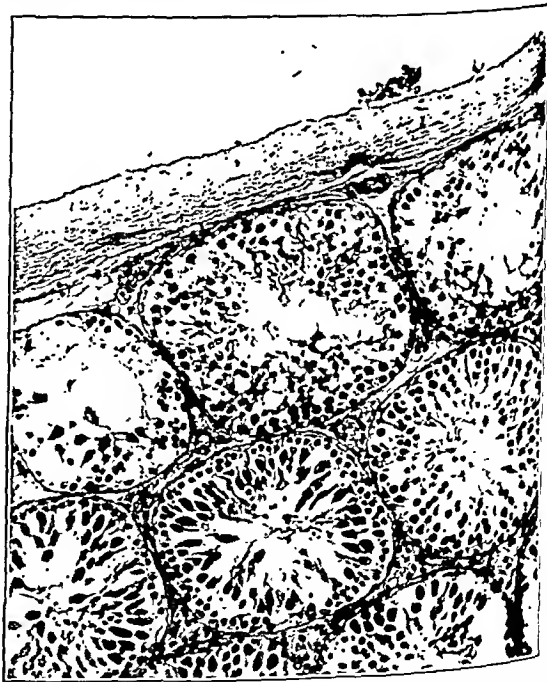


Fig. 5.—Section of cryptorchid testes from an untreated animal. Note slight reduction in spermatogenesis as compared with figure 4. Hematoxylin-eosin stain, $\times 140$.

Before detailing the results of our experiments with anterior pituitary-like substance, we shall state our experience in the surgical correction of testes of patients

6. Mimpriss, T. W.: Treatment of Imperfect Descent of Testis with Gonadotropic Hormone, *Lancet* 1: 497-499 (Feb. 27) 1937.
7. Cabot, Hugh: Management of Patients with Retained Testes, *Radiol. Rev. & Mississippi Valley M. J.* 58: 198-203 (Nov.) 1936.
8. Cole, H. H.: On Biological Properties of Mare Gonadotropic Hormone, *Am. J. Anat.* 59: 299-331 (July) 1936.

9. Counsellor, V. S.: Cryptorchidism: Treatment and Results in 111 Cases, *J. Urol.* 30: 327-343 (Sept.) 1933.
10. Walters, Waltman, and Thiessen, N. W.: Cryptorchidism, *Proc. Staff Meet., Mayo Clin.* 10: 132-139 (Feb. 27) 1935.

who had received endocrine therapy. In the seven cases in which the larger dosage, or over 6,000 rat units, was given the testis was much smaller than in untreated cases or in those in which the smaller dosage was given.

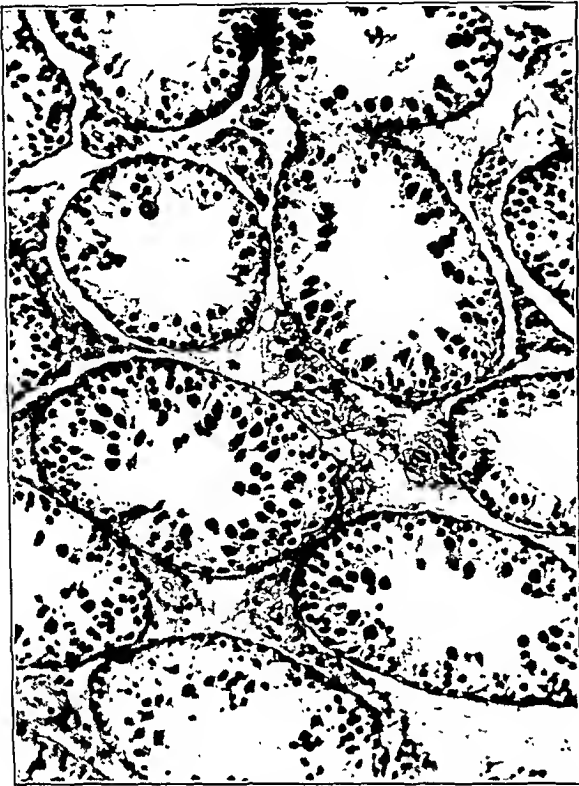


Fig. 6.—Section of cryptorchid testes from a treated animal. Note marked reduction in spermatogenesis and edema of interstitial tissue. Hematoxylin-eosin stain, $\times 140$.

There was no exception to this rule. The surgical correction was much more difficult on account of the increased number and thickness of the adhesions

TABLE 2.—Average Weights of Testes in Treated and Untreated Groups

	Normally Situated Testes (Weight in Milligrams)	Cryptorchid Testes (Weight in Milligrams)
Rats received 200 rat units of anterior pituitary-like substance of pregnancy urine, total dosage	1,576	764
Rats received no hormone.....	1,510	678

encountered. The adhesions were not only profuse about the vessels of the cord and the component fascial and muscular structures but even around the testis itself, a condition not commonly observed by us in cases in which treatment was not given. Proper surgical correction of undescended testes depends largely for its success on a meticulous dissection and the removal or severance of fibrous bands, which are always present. Therefore the increased number and thickness of these bands make the operation in our hands much more difficult and time consuming. This view does not seem to be in agreement with that expressed by others.

Naturally we have not removed the testis in any of the aforementioned cases regardless of the degree of

apparent degeneration and so cannot report on their microscopic appearance. As these all occurred in boys under 14 years of age, we hoped that regenerative processes might possibly take place after the cessation of endocrine therapy and the proper placement of the testis into the scrotum. Some testes, however, appeared to be so badly damaged that we have but little expectation of this taking place.

EXPERIMENTAL. METHOD

Forty male albino rats were used in this study. They were all subjected to similar treatment and were similarly controlled. Among the last fifteen injected there were three groups of rats, each group consisting of litter mates, and we decided that in these groups our results would be most accurate and conclusive and therefore will detail only the results in this series. However, the results in the first twenty-five were similar to the groups consisting of litter mates.

All rats were made unilateral cryptorchids on the thirtieth day of life; the right testicle of each animal was left in its normal position. (In rats it is possible to render the animal cryptorchid with a minimum of trauma to the testis; in fact, practically by atraumatic operation.) In the first twenty-five rats injections of 50 rat units of anterior pituitary-like substance was given, in one group on the day following operation and in another on the thirty-first day after operation. Each



Fig. 7.—Cryptorchid testes from a treated animal. Note marked thickening of the capsule and leukocytic infiltration. Hematoxylin-eosin stain, $\times 140$.

treated animal received 50 rat units a week for four injections. Controls for each series were carefully examined.

In the group of fifteen rats which was divided into groups of litter mates, the weights of the normally placed and the cryptorchid testes in the treated and

the untreated animals are shown in table 1. Group A consisted of five animals, three of which were injected and two were used as controls. Group B numbered six animals, five of which received injections and one was used as a control. Group C numbered four animals, three of which were injected and one was used as a control. The treated animals in this series also received 50 rat units of anterior pituitary-like substance at weekly intervals for four weeks, thus receiving a total dosage of 200 rat units. All animals were killed six weeks after the last injection of anterior pituitary-like substance. The testes were immediately removed, weighed and promptly fixed in 10 per cent solution of formaldehyde. Sections were embedded in paraffin and were stained with hematoxylin and eosin.

MICROSCOPIC EXAMINATIONS

Normally Situated Testes.—In both the injected and the control animals the normally situated testes showed no appreciable changes. The average weights for the normally situated treated animals closely approximated one another (tables 1 and 2). Furthermore, the administration of the hormone had no effect on spermatogenesis or on the interstitial tissues, as was seen in the cryptorchid testes. Active spermatogenesis was seen in the normally situated testes of all the treated animals and their capsules, and the interstitial tissue showed no changes.

Cryptorchid Testes.—All the cryptorchid testes, both treated and untreated, showed striking anatomic changes. These, however, were most marked in the animals injected with anterior pituitary-like substance. They may be divided into four groups: (1) changes in the capsule, (2) changes in the interstitial tissue, (3) changes in the seminiferous tubules and (4) alterations in weight.

1. Changes in the Capsule: These were observed only in the animals injected with anterior pituitary-like substance. At autopsy dense fibrous adhesions were grossly recognized between the visceral and the parietal layers of the tunica vaginalis, and the tunica albuginea was markedly thickened. Microscopically the thickened capsule was seen to be diffusely infiltrated with small round cells, intermingled with which were occasional polymorphonuclear leukocytes. Many young newly formed blood vessels were also seen. These changes were not observed in the cryptorchid testes of the uninjected control animals.

2. Changes in the Interstitial Tissue: The interstitial tissue in the cryptorchid testes, both in the treated and in the untreated animals, appeared to be increased in amount. In many of them there was considerable edema of the interstitial tissue, the cells of Leydig and other cellular elements being suspended in a pale, eosinophilic liquid. This was most marked in the animals that had been given the hormone. In some of these animals there was also an increased vascularity of the interstitial tissue.

3. Changes in the Seminiferous Tubules: The most striking microscopic changes observed in these testes were seen in the tubular epithelium. These changes consisted in a decrease in the number of the sex elements and failure of their development. This was seen in both the treated and the untreated cryptorchid testes but was much more marked in the former. Spermatids and mature sperms were seen occasionally in the cryptorchid testes of untreated animals but never

in the treated ones. The tubules of the latter appeared shrunken and atrophic. Mature sperms were completely absent, the tubules being filled with Sertoli cells and spermatogonia. Occasionally the tubules were partially collapsed and in their lumens only remnants of sex cells were visible. Occasional partially or completely hyalinized tubules were seen throughout the sections. Similar but less marked changes were observed in the untreated cryptorchid testes. The tubules of the latter contained many spermatogonia and spermatocytes and occasionally mature sperms. Hyalinization of these tubules was not observed.

4. Alterations in Weight: The changes in the weights of the testes from the treated and the untreated animals are presented in tables 1 and 2. The normally situated testes in both the treated and the untreated animals weighed approximately the same. There is, however, some variation in the weights of the cryptorchid testes in the treated and untreated groups. The average weight of the former is 764 mg. and of the latter 678 mg., a difference of 12 per cent. This increase in the weight of the cryptorchid testes is probably due to the edema and hyperplasia of the interstitial tissue in the testes of these animals.

SUMMARY AND CONCLUSIONS

The careful evaluation of the position of the abnormally situated testis, which can be determined by painstaking examinations, is necessary. The group of abnormally situated testes which invariably will descend when they reach or approach adult size and weight are to be differentiated clinically from the group of true undescended and ectopic testes. True undescended and ectopic testes always require operative treatment for their correction. Retractable testes may descend spontaneously as late as the seventeenth year. Gonadotropic substance has no value in the preoperative care of true undescended and ectopic testes. Its routine use in retractile testes is not recommended. Gonadotropic substance is definitely harmful in larger dosage to testes which have not reached the scrotum. Experimental animals have shown a characteristic response to endocrine therapy when the testes have been made cryptorchid. The gross appearance of these testes corresponds closely to that of undescended testes in which a larger dosage of hormone had been received and in which operation was subsequently required to overcome a mechanical cause for the failure of the testes to reach the scrotum. Operation was done in a series of seven clinical cases showing marked evidence of degeneration after the use of hormone. The surgical correction of the undescended testis after endocrine therapy is not facilitated, as claimed by others, but is rendered more difficult.

25 East Washington Street.

Good Companions.—Parental example is probably the greatest single factor in training. What you yourself do is of greater influence than anything you can say especially if your actions belie your words. Your children will inevitably desire to be like you and to act like you. The pull is far stronger than the mere conscious desire alone. The imitative impulse, appearing about the time a child learns to talk, acts both intentionally and unconsciously as a highly developed, automatic reinforcement in the copying of mothers' and fathers' habitual conduct and emotional attitudes.—Hohman, Leslie B., *As the Twig is Bent*, New York, Macmillan Company, 1940.

Clinical Notes, Suggestions and New Instruments

SUBACUTE ENDOCARDITIS AND SYSTEMIC MYCOSIS (MONILIA)

HENRY JOACHIM, M.D., AND SILIE H. POLAYES, M.D., BROOKLYN

As far as could be ascertained, no case of subacute bacterial endocarditis with systemic mycosis due to *Monilia* recognized during life has ever been reported in the literature. Dr. Emanuel Libman, who saw this case with us, referred us to a recent report by Friedman and Donaldson.¹ In their case nests of yeastlike cells were isolated from the aortic vegetations on postmortem examination of a patient who died of subacute bacterial endocarditis. However, the authors were unable to isolate the organism clinically or identify it on postmortem examination. Because of the rarity of this condition and the circumstances under which the infection occurred in our case, it was considered worthy of publication.

REPORT OF CASE

History.—F. M., a white man aged 48, American born, married, a bookkeeper, was admitted to the surgical service of the Cumberland Hospital on April 24, 1939, because of midabdominal pain of two days' duration.

The patient had been addicted to the use of morphine and heroin for twenty years. For eighteen months he had injected the drug intravenously. In the parlance of addicts, he was known as a "main line shooter." The technic of the intravenous injection consisted in filling a medicine dropper with a solution of morphine or heroin, attaching a hypodermic needle to the dropper and injecting the solution into the basilic vein of the left arm once daily. No aseptic or antiseptic cautions were observed. It was difficult to establish the daily dose administered, since the drugs were illicitly procured from narcotic vendors who probably "thinned out" the amount sold. The patient was of the opinion that he used from 20 to 40 grains (1.3 to 2.6 Gm.) daily.

The patient averred that in January 1939 he ceased the use of the drugs on account of his financial inability to secure them and submitted himself for the treatment of his drug addiction. Since that time, he stated, he had absolutely refrained from the use of narcotics. He suffered from withdrawal symptoms such as salivation, joint and muscle pains, abdominal cramps and diarrhea. These symptoms persisted and he was treated for "rheumatism." He began to lose in weight and became progressively weaker. Fever developed. Two days prior to his admission to the hospital he took a sun bath for an hour. This was followed by a drink of orange juice. One hour later severe crampy pains developed in the upper part of the abdomen. These were accompanied by vomiting. The pains continued and spread to the lower part of the abdomen. Vomiting persisted with inability to retain any food or fluids. A surgical condition was suspected, for which he was admitted to the surgical wards of the hospital.

In 1910 the patient had an attack of gonorrhea without complications. He had diphtheria twelve years before admission. About seven years before admission he had been told that he had a heart murmur and about three years before admission he had pneumonia. Several months prior to admission, while being treated for his narcotic addiction, he was supposedly suffering from "rheumatism."

He smoked twenty cigarettes daily and indulged only moderately in liquor.

The patient's father died of tuberculosis at the age of 35. Otherwise the family history was irrelevant.

Physical Examination.—On admission the patient's temperature was 102.6 F., pulse rate 114, respiratory rate 28 and systolic blood pressure 90. He was cachectic and had a sallow com-

plexion. The pupils were regular and equal and reacted to light and in accommodation. The eyegrounds were normal. The heart was not enlarged to percussion. The rhythm was regular. A loud rough aortic systolic murmur was present. This could be auscultated over the entire chest anteriorly and was transmitted upward into the vessels of the neck. The aortic second sound was muffled. The abdomen was diffusely tender to palpation. Rigidity was not present. The liver edge was palpable about two fingerbreadths below the costal margin. It was soft and not tender. The spleen was palpable but not tender. No cyanosis or edema was noted. There was slight clubbing of the extremities. Along the course of the left basilic vein there was a streak of brown pigmentation.

Course.—May 3 a tender nodule appeared on the left palm (Osler node). Petechiae were noted in the conjunctivas, scrotum, left thigh and right inguinal region. May 7 it was noted that the cardiac murmur was intensified. May 9, sternal tenderness was elicited. May 13 the right eye became tender. Ophthalmologic examination showed no abnormality. May 14 the patient had a severe chill. His temperature was of the septic type with repeated chills. This was accompanied by fleeting joint and muscle pains. There were swelling and redness of

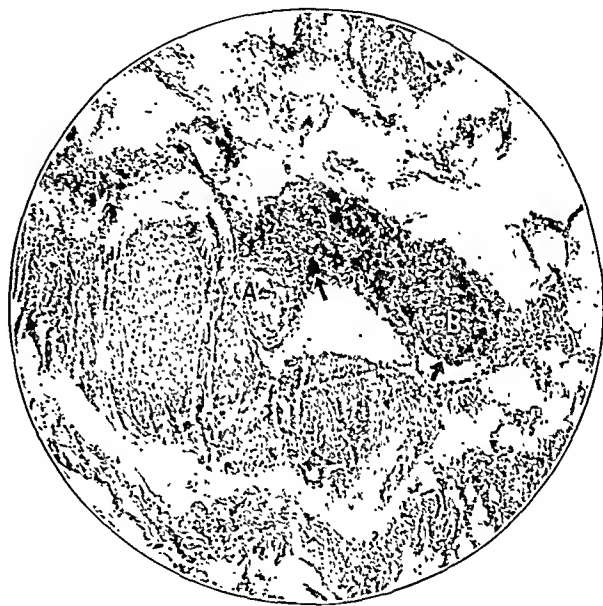


Fig. 1.—Medium power magnification of a granulomatous lesion in the subcutaneous tissue of the elbow. Note the huge foreign body giant cell (A) and large mononuclear cells accompanied by a marked fibroblastic reaction (B) about deposits of iron-free debris (arrows). *Monilia* organisms may be discerned with difficulty among the infiltrating cells. Reduced from a photomicrograph with a magnification of 110 diameters.

the joints. The spleen enlarged rapidly and was painful and tender. Tender nodules developed on the soles of the feet. The patient became progressively weaker and died on June 13.

Laboratory Examinations.—Five blood counts were made between April 25 and May 30. The hemoglobin content varied between 66 and 70 per cent. The erythrocytes ranged between 3,500,000 and 4,300,000, while the leukocytes varied between 6,750 and 10,600 per cubic millimeter. The differential smears showed from 60 to 73 per cent polymorphonuclears, 17 to 31 per cent lymphocytes, 2 to 10 per cent monocytes, 0 to 2 per cent eosinophils and 0 to 1 per cent basophils.

The sedimentation rate varied from fifteen minutes to two hours for 18 mm.

The urine frequently showed traces of albumin, occasionally fine as well as coarsely granular casts, white cells and red cells.

Bacteriologic Study.—A total of eleven blood cultures were made. The first, on May 3, and each subsequent culture showed the presence of innumerable colonies of yeastlike cells.

Throat, stool and urine cultures failed to show any fungus. Cultures of the contents of the container from which the drugs were injected showed organisms identical with those obtained from the blood.

From the Departments of Medicine and Pathology of Cumberland Hospital.

Miss Florence Bittman of the Bacteriology Laboratory of Bellevue Hospital aided in the bacteriologic examinations.

1. Friedman, N. B., and Donaldson, Lillian: Subacute Endocarditis with Systemic Mycosis, Arch. Path. 27: 394 (Feb.) 1939.

Biopsy.—The vein into which the drug was injected revealed the following features:

Macroscopically the specimen consisted of skin about 1 cm. in its greatest dimension and a section of a vein about 4 cm. in diameter. The epidermis and subcutaneous tissue were speckled with numerous areas of blue-black pigmentation. A silk ligature was found tied about one of the small veins.

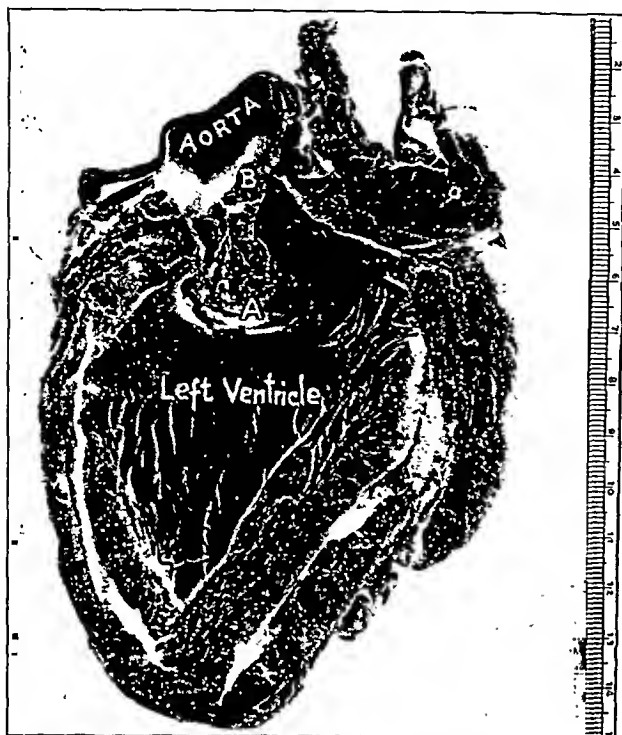


Fig. 2.—Left ventricle opened to expose the aortic valve and vegetations. Almost the entire right posterior aortic cusp (A) is destroyed by the vegetations (colonies of *Monilia*). Note the apex of vegetations (B) extending 4 cm. above the aortic ring.

On microscopic examination the skin and subcutis showed numerous deposits of iron-free, nondescript particles and fibrosis. Many of the particles were being engulfed by foreign body giant cells or surrounded by a reactive inflammatory zone, the infiltrates of which consisted predominantly of mononuclear and plasma cells. Occasional yeastlike cells were demonstrable among the infiltrating cells and in the interstices. Although the changes just described were demonstrable in the perivascular connective tissue, the vessel walls proper showed no changes.

The diagnosis was foreign body granulomas of the skin and subcutaneous tissue.

X-ray examination of the chest revealed clear pulmonary fields. The heart was mitral in configuration, not enlarged but with a marked elongation and tortuosity of the aorta.

Bacteriologic Description of the Organism.—Morphology: The organism was ovoid and averaged about 4 microns in diameter; there were atypical short mycelia. One of the Sabouraud subcultures showed distinct hyphae.

Staining Reaction: The organism was gram positive except for some of the mycelia, which stained pink.

Reproduction: This occurred by budding.

Cultural Characteristics: Nutrient, dextrose and blood agar mediums showed opaque yellow convex round nonhemolytic colonies after from forty-eight to seventy-two hours. The temperature of incubation was 37.5 C.

Stab culture on Sabouraud's medium yielded an inverted fir tree type of growth. In broth there were heavy sediment and slight cloudiness of supernatant fluid after seventy-two hours' incubation. In gelatin no liquefaction occurred.

Sugar reactions were as follows: There was no acid or gas in lactose and mannite. There were acid and about 10 per cent gas in maltose, saccharose and dextrose.

The provisional diagnosis was moniliasis.

Serologic Examination.—Agglutination tests performed with the fungus recovered from the blood culture and the patient's serum gave the following reactions:

Serum dilution 1:10, marked agglutination in five minutes.

Serum dilution 1:100, definite agglutination in twenty minutes.

There was no agglutination with saline solution or with normal human serum control.

The patient's serum agglutinated known cultures of *Monilia albicans* to a dilution of 1:640.

The bacteriologic as well as the serologic data conform to the general description of the *Monilia* group. Final complete identification must await further cultural differentiation.

Necropsy.—This was performed six hours post mortem.

General Examination: The body was emaciated. The flexor surfaces of both elbow regions were dotted with minute blue areas. The left cubital fossa presented a healed wound of a recent biopsy. Microscopic examination of the pigmented areas disclosed accumulations of nondescript iron-free black particles, many of which were engulfed by giant phagocytes and about which granulomatous changes were present, characterized by an abundance of foreign body giant cells (fig. 1). The granulomas involved perivascular lymphatics of the subcutaneous tissue and adjacent perimysium. In these areas were large mononuclear cells more than twice the size of the ordinary leukocyte. They contained hyperchromic round nuclei which occupied the major portion of the cell body. Throughout the inflammatory zones were numerous monilia organisms occurring singly or in small groups.

Sections of the median basilic and cephalic veins, as well as of the brachial arteries, failed to show any changes.

Cavities: The peritoneal cavity presented recent perisplenic and old perihepatic adhesions. Each pleural cavity contained 100 cc. of sanguineous fluid. There were also bilateral dense fibrous pleurodiaphragmatic adhesions. The pericardial cavity contained a slightly increased amount of fluid.

Cardiovascular System: The heart weighed 330 Gm. There were patches of fibrinoplastic exudate on the epicardium of the right atrium, the auricular appendage and the anterior

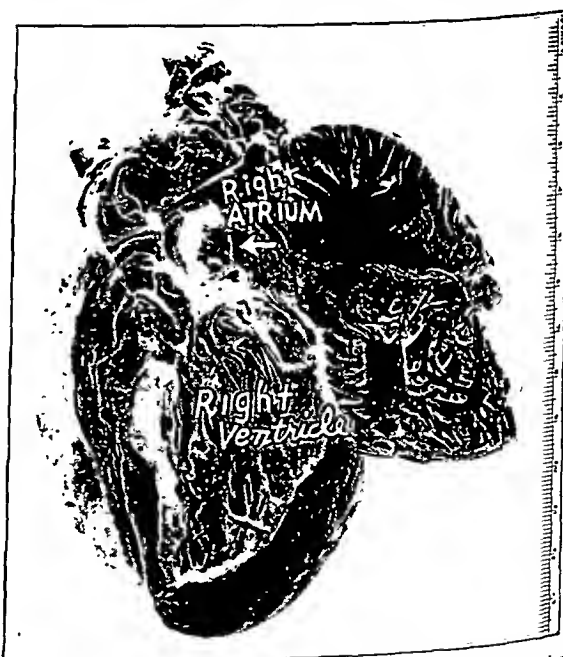


Fig. 3.—Right side of the heart exposed, showing the bulging, fluctuating mass of necrotic tissue and *Monilia* colonies perforating through the atrial wall just above the medial cusp of the tricuspid valve (arrow).

surface of the right ventricle. The myocardium of the left ventricle presented numerous scars, some of which involved the epicardium. The right posterior cusp of the aortic valve was almost completely replaced by a cauliflower-like gray pyramidal mass of vegetations which were engrafted on the base of the aortic cusp. The apex of the mass projected into the lumen of the aorta, 4 cm. above the aortic ring (fig. 2). At the

base it was continuous with a fluctuating mass of necrotic structure which bulged into and perforated the wall of the right atrium just above the medial cusp of the tricuspid valve (fig. 3).

Microscopic examination revealed the presence of a pancarditis. The epicardium at the sites mentioned showed an acute inflammatory process. The infiltrate contained many of



Fig. 4.—High power magnification of aortic vegetations. Note the reactive zone of mononuclear cells and fibroblasts at the base of the valve (A) and massive colonies of *Monilia* (B) held together by a fibrin network (C). Reduced from a photomicrograph with a magnification of 150 diameters.

the large mononuclear cells previously described. There was also an acute interstitial myocarditis (focal in some areas, diffuse in others) superimposed on an already existing extensive myofibrosis. The aortic vegetations were composed of a layer of fibrin and exudate covering massive colonies of *Monilia*. The latter constituted the major portion of the vegetations and in areas penetrated the fibrin layer. At the attachment of the mass to the aortic ring there was a reactive zone accompanied by fibroblasts in palisade arrangement and large cells (fig. 4). Beneath this layer there was marked calcium deposition. The mitral valve showed only fibrinous thickening. *Monilia* organisms occurring singly and in groups were demonstrable in all sections.

The aorta showed moderate atherosclerosis. The superior mesenteric artery, 3 cm. distal to its celiac junction, presented a globular aneurysm 1.2 cm. in diameter. Its intimal layers were dissected by a hematoma which was continuous with a layer of fibrin thrombus replacing intima. The adjacent media and adventitia showed arteritis with an infiltrate consisting mainly of small lymphocytes and large mononuclear cells.

The splenic artery showed occlusion of one of its middle hilar branches by a fresh thrombus.

The right renal artery presented a similar thrombus in one of its anterior branches.

Respiratory System: The larynx, trachea and bronchi were filled with sanguineous fluid. The lungs were voluminous and red. Bloody fluid flowed freely from their cut surfaces. Sections revealed areas of red hepatization alternating with areas of edema and emphysema. *Monilia* organisms were demonstrable in the exudate, which was predominantly of the mononuclear cell type.

Gastrointestinal System: The oral cavity was normal. The stomach was hugely distended. The rest of the tract showed only occasional mucosal hemorrhages.

Spleen: The organ weighed 780 Gm. and presented fibrinous perisplenitis. A thrombus in one of the middle hilar branches of the splenic artery had produced a nonsuppurative infarct which involved the entire midzone of the splenic parenchyma, from the anterior to the posterior margin and appeared across

the entire diaphragmatic surface as a band of gray discoloration about 3 cm. in width. The pulp was hemorrhagic and the malpighian corpuscles were reduced in size. The parenchyma contained many large mononuclear cells similar to those already described. The sinuses were distended, many being filled with numerous myeloid cells and large phagocytes with ingested nuclei and red cells (fig. 5). Groups of *Monilia* were demonstrable throughout the section and numerous colonies of these were found in thrombi occluding the vessels.

Pancreas: This organ weighed 150 Gm. and was essentially normal.

Biliary System: The liver weighed 1,735 Gm. The right lobe extended almost to the pelvic brim. Sections showed acute hepatitis. The infiltrate was periportal in distribution and consisted mainly of large mononuclear cells. A calcified encapsulated (parasitic?) cyst resembling *Pentastoma denticulatum* was found beneath Glisson's capsule of the right lobe. The rest of the biliary tract, including the gallbladder and bile ducts, showed no changes.

Urinary System: The right kidney weighed 165 Gm. and the left 150 Gm. The organs were moderately arteriosclerotic. Both showed small nonsuppurative infarcts caused by emboli composed of colonies of *Monilia* in a number of the smaller branches of the renal arteries (fig. 6). There were also foci of interstitial nephritis in which were numerous large mononuclear cells. Deposits of calcium were present in the tubules and interstices of the apical portions of some of the pyramids. A discrete small area of gray discoloration noted in the cortex of the right kidney was found to be a papillary adenoma of tubular origin. The rest of the urinary tract showed nothing remarkable.

Lymphatic System: The axillary and periaortic lymph nodes presented sinuses distended with large phagocytes and congested vessels. *Monilia* was demonstrable in sinuses and interstitial tissue.

Genital, Endocrine and Skeletal Systems: No changes were noted.

Central Nervous System: The brain weighed 1,400 Gm. Portions of the anterior frontal, posterior occipital and right temporal lobes showed brown discoloration of the meninges due

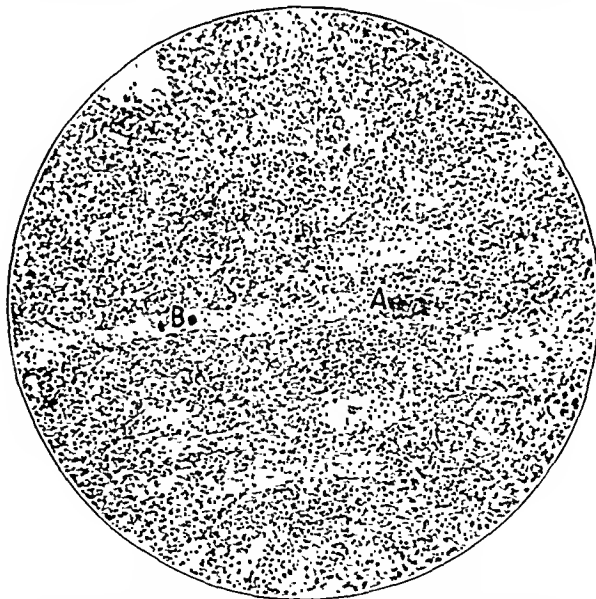


Fig. 5.—Representative section of spleen showing the characteristic large mononuclear cells (A) and myeloid cells (B) in distended sinuses. Reduced from a photomicrograph with a magnification of 150 diameters.

to hemorrhage. These areas showed an intense inflammatory reaction in the meninges. In the infiltrate were found many mononuclear cells and occasionally *Monilia*. The inflammatory process followed along blood vessels deep into brain tissue, where minute abscess-like collections of exudate were demonstrable (fig. 7). The choroid plexus showed perivascular collections of mononuclear cells.

The spinal cord showed foci of hemorrhagic extravasation into the anterior cornua.

The eyes showed occasional petechiae in the conjunctiva and eyegrounds, including the optic disks.

Bacteriologic Examination: Vegetations of Aortic Valve. Direct smear showed budding fungi. Culture showed *Monilia*, *Streptococcus nonhaemolyticus* and *Bacillus coli*.



Fig. 6.—High power magnification of kidney showing mycotic emboli occluding smaller branches of renal arteries. Reduced from a photomicrograph with a magnification of 150 diameters.

Pericardial Fluid. Direct smear showed a few small chains of streptococci. Culture showed *Streptococcus nonhaemolyticus* and *B. coli*.

Abscess of Right Atrium. Direct smear showed budding fungi. Culture showed *Monilia* and *B. coli*.

The anatomic diagnosis was: 1. *Monilia* endocarditis; fibrosis and calcification of the aortic valve. 2. Acute interstitial myocarditis and pericarditis; myofibrosis cordis. 3. Infarcts of spleen and kidneys. 4. Hemorrhagic pneumonitis. 5. Acute hepatitis. 6. Meningo-encephalitis and hemorrhages of spinal cord. 7. Aneurysm of superior mesenteric artery. 8. Subcutaneous foreign body granulomas of upper extremities.

COMMENT

This case presents a number of interesting features. Besides being unique clinically, it also offers a number of problems which still remain unsolved. The absence of any demonstrable changes in the large veins into which the patient was purported to have injected the drugs leaves one in doubt as to the exact course followed by the *Monilia* organisms from their port of entry in the skin. Clinically it was considered likely that a mycotic granuloma of an infected vein of the forearm acted as the focus of infection which produced the systemic mycosis. However, the granulomas described cannot be considered as reaction to *Monilia* for two reasons: First, the granulomatous lesions were observed in the skin only at the sites of the needle punctures and not elsewhere in the tissues, where the *Monilia* organisms were found to be even more prevalent than in the skin. Second, the lesions appeared to be merely foreign body giant cell reactions to the debris which was introduced into the subcutaneous tissue with the needle. It is more probable, therefore, that the *Monilia* organisms gained access to the circulation (and thence to the aortic valve) or directly to the blood stream with the insertions of the needle into the lumen of the vein, but without producing any granuloma in the latter.

Another interesting problem is the question of primary infection. It is not possible to determine with any degree of certainty whether *Monilia* was the primary etiologic agent

which produced the aortic lesion. Few small chains of streptococci observed on direct smear of the pericardial fluid, as well as the nonhemolytic streptococcus in the cultures obtained from the vegetations, suggest the possibility of a preexisting streptococcal infection in the aortic valve with a superimposed infection by *Monilia*. However, the presence of *B. coli* along with the streptococci in the postmortem cultures of the vegetations and pericardial fluid points to the greater likelihood that the streptococcus was a postmortem, rather than a primary, invader. This view is strengthened by the facts that morphologically and in the tissue sections only *Monilia* was demonstrable in the vegetations and that streptococci could not be recovered from any of the numerous blood cultures which were made during life, all of which showed pure cultures of *Monilia*.

The immunologic aspects of this case are intriguing. The patient's serum gave positive reactions with known cultures of *Monilia albicans*, although culturally the organism answers more to the description of *Monilia psilosis*. However, the final identification of the organism has not yet been made. The agglutinative titer of the patient's serum before death was high, dilutions of 1:100 having clumped in less than twenty minutes the suspensions of *Monilia* which had been recovered from the patient's own blood.

The nature of the more pertinent histologic changes in this case are also worthy of emphasis. The changes which were observed throughout the tissues, although not pathognomonic, are characteristic. The outstanding feature of the inflammatory infiltrate was the peculiar monocytic response. The splenic pulp and sinuses, the pulmonary alveolar exudate, the reactive zone at the base of the aortic valve and even the infiltrating cells in the periphery of the granulomas all showed a monotonous type of large monocyte as the predominating element of the infiltrate. The reaction resembles the tissue response observed early in virus infections, rheumatic fever, influenza and related diseases. Aside from the occasional *Monilia* organisms present in the tissues, no definite changes were observed which could be interpreted as characteristic of a fungus infection.

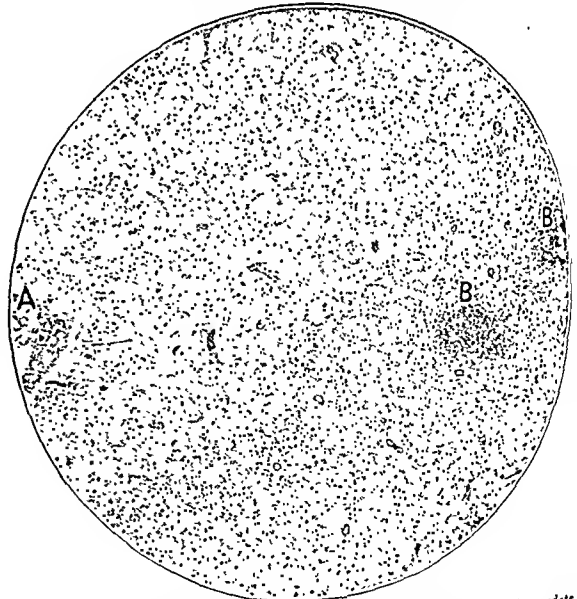


Fig. 7.—Section through the frontal lobe showing meningeal exudate (A) and abscess-like collection of exudate (B) in the deeper cerebral tissue. Reduced from a photomicrograph with a magnification of 60 diameters.

SUMMARY

1. A rare case of subacute endocarditis with systemic mycosis (*Monilia*) was observed.
2. Various problems were presented by the histologic, bacteriologic and immunologic studies of this case.
3. No similar case could be found in the literature.

871 Park Place.

A CASE OF ARSENIC PERIPHERAL NEURITIS
TREATED WITH SYNTHETIC VITAMIN B₆
AND ALPHA-TOCOPHEROLR. W. VILTER, M.D.; C. D. ARING, M.D., AND T. D. SPIES, M.D.
CINCINNATI

This report¹ concerns observations on the effect of parentally administered vitamin B₆ and alpha-tocopherol in a case of arsenic peripheral neuritis which had been treated unsuccessfully with thiamine hydrochloride.

S. A., a salesman aged 35 who had been in good health, was admitted to the Cincinnati General Hospital on Nov. 28, 1939, with acute arsenic poisoning following the ingestion of a teaspoonful of "rat embalmer" (arsenic trioxide). Vomiting and diarrhea subsided after a week of hospitalization and general supportive therapy. At the end of the second week he complained of numbness and tingling sensations in his hands and right foot. (His left leg had been amputated traumatically in 1930).

Stabbing and cramping pains appeared in his hands and the calf of his right leg and became so severe that he was unable to rest. His hands became so weak that he could not pick up small objects. The skin of his hands, forearms, foot and leg were extremely hyperesthetic to stroke and to pinprick and anesthetic to light touch with cotton. Definite "afterglow" of unpleasant sensation followed rather light stroking of the palms of his hands. Motor power in his hands was reduced to 20 units (normal from 130 to 200 units), as measured by a spring type of dynamometer. The deep reflexes were absent in the leg and hypo-active in the arms. He noted that his upper extremities were considerably more painful and weak than his lower.

Routine laboratory tests, including examination of cerebrospinal fluid, gave negative results. Analysis of the hair, finger nails and toe nails for arsenic, performed by Dr. Robert A. Kehoe of the Kettering Laboratory of Applied Physiology of the University of Cincinnati, showed the following values of arsenic trioxide: distal hair, 1.1 mg. per hundred cubic centimeters; proximal hair, 7.7 mg.; toe nails, 9.1 mg.; finger nails, 4.7 mg. (normal hair and nails = 0.1 mg. or less).

The patient was treated with 50 mg. daily of thiamine hydrochloride in physiologic solution of sodium chloride, intravenously for three weeks after the onset of the neuritis, without influencing the condition. After administration of thiamine was discontinued, the patient was given 50 mg. of alpha-tocopherol intramuscularly twice daily for one week, with no subjective or objective improvement. Then, 20 mg. of synthetic vitamin B₆ in sterile physiologic solution of sodium chloride was given intravenously twice a day for three days. Within four hours after the first injection, the patient volunteered that his discomfort was much less than at any time since the onset of his illness. During this three day period there was a striking increase in strength (from 20 to 60 units), as measured in dynamometer units, and a decrease in hyperesthesia, deep pain and cramping sensations. A relapse to the original level of discomfort and weakness occurred when injections of physiologic solution of sodium chloride were substituted for the vitamin B₆. Relapses following the substitution of saline solution or thiamine hydrochloride for vitamin B₆ and remissions when vitamin B₆ was readministered were observed three times during the next six weeks. Vitamin B₆ was the only substance which caused a remission, but improvement was more spectacular and rapid when alpha-tocopherol, 50 mg. intramuscularly, was given in conjunction with vitamin B₆. Ten weeks after the onset of peripheral neuritis all medication was discontinued, and the patient was discharged from the hospital. His strength was almost normal (110 dynamometer units); he had no pain or hyperesthesia but his hands and his foot were hypesthetic to pinprick and light touch. Follow-up examination three weeks later showed the same evidence of chronic nerve damage as was present at discharge.

From the Departments of Internal Medicine and Neurology, University of Cincinnati College of Medicine. These studies were aided by a grant from the Rockefeller Foundation.

1. Since cases of peripheral neuritis due to arsenic are rare, we feel that these encouraging results should be known so that other investigators may assess the effectiveness of these vitamins in similar cases.

SUMMARY

Partial remission of a severe polyneuritic syndrome due to arsenic was induced rapidly with vitamin B₆. A relapse occurred on each of three occasions when thiamine hydrochloride or physiologic solution of sodium chloride was administered, and vitamin B₆ discontinued. The most spectacular remissions occurred when vitamin B₆ and alpha-tocopherol were administered concurrently. To maintain the improvement, these substances had to be administered daily.

HEMANGIOMA OF THE GASTROINTESTINAL TRACT

PERRY N. PIEROSE, M.D., LOS ANGELES

This report includes the record of one case in which hemangioma of the gastrointestinal tract was proved and a review of the literature concerning this condition. This case is of particular interest because the symptoms were of fifteen years' duration and were severe from the onset and because of the eventual correct diagnosis and successful treatment.

REPORT OF CASE

History.—A woman aged 40, a Caucasian, had been told that during the three days following birth she passed stools which contained bright red blood; this significant fact in her past history should perhaps be emphasized at this point. A summary of the history reveals that the first symptom of her present condition came on rather suddenly in 1926 when she was 29 years of age and consisted of great weakness. This was followed by pallor, tarry stools and "extreme anemia." The symptoms developed suddenly, were not accompanied by pain and subsided while the patient rested in bed at home; she did not call a physician at this time. Following this experience she was admitted to the Los Angeles County Hospital six times during the next thirteen years. On each admission the characteristics of her condition were those already enumerated. Following each of these episodes the patient's condition would improve, apparently as a result of bed rest, transfusions with whole blood, a well balanced, adequate diet and administration of iron. The diagnosis was at all times indefinite and uncertain and the cause of her condition remained obscure and unexplained. Exploratory laparotomy was done in 1932 and again in 1933, but the cause of her symptoms was not found.

The experience that brought the patient to the hospital at the time of her last entry, Feb. 10, 1939, was a repetition of the symptoms and changes that characterized all her attacks. There was no history of intolerance of any food, epigastric distress, chest pain, chills, night sweats or loss of weight.

Examination.—The patient was well developed, well nourished and extremely pale; she did not appear to be in distress but gave the impression of being very sick. She was rational and cooperative. Her temperature was 99 F., pulse rate 130, respiratory rate 26 and blood pressure 116 systolic, 84 diastolic. Routine examination of the head revealed no abnormalities of note. Chest resonance, breath sounds and the size of the heart were within normal limits. A soft systolic murmur was heard at the apex. Two old healed surgical scars were present in the epigastrium. There was no abnormal tenderness or rigidity of the abdominal wall. The liver, kidneys and spleen were not palpable and no abnormal masses were found. Peristalsis was normal. Examination of the external genitalia, pelvis, rectum, spine and superficial lymph glands revealed no noteworthy abnormalities. The extremities were well proportioned and symmetrical. Petechiae or other discoloration of the skin was not found. The reflexes were normal.

Laboratory examinations revealed hemoglobin 18 per cent (Sahli), erythrocytes, 1.7 million, leukocytes 16.6 thousand and of normal distribution. The urine showed no albumin or sugar and microscopic examination gave essentially negative results. The blood Wassermann and Kahn reactions were negative. The stool gave a strongly positive reaction for occult blood.

Immediate treatment consisted of transfusions with whole blood, a general diet and iron by mouth; improvement was remarkable, but the stools continued to give positive reactions for occult blood.

From the Medical and Surgical Services of the University of Southern California School of Medicine in the Los Angeles County Hospital.

Summary of Admissions.—From the time of onset of symptoms in 1926 she frequently experienced weakness, passed tarry stools and became pale. These were her complaints when she entered the Los Angeles County Hospital for the first time, Dec. 12, 1932. She was weak and pale. The blood pressure was 120 systolic, 80 diastolic, hemoglobin content 35 per cent (Sahli), erythrocyte count 1.9 million, leukocyte count 10,000 and differential normal. The urine was normal. By x-ray examination of the gastrointestinal tract the duodenum was considered to be slightly enlarged, passage of barium sulfate through it was somewhat delayed, and it was suggested that these changes might result from the presence of a duodenal polyp. An enema of barium sulfate revealed no abnormalities of the colon.

Exploratory laparotomy was performed and a peculiar band was found along the antemesenteric border of the jejunum, which produced in it an appearance similar to that seen in the large intestine. Sacculations containing enlarged blood vessels and engorgement of the smaller vessels were found in the lateral walls of the jejunum. Careful examination of the duodenum revealed no indication of polyp or ulcer. The diagnosis on discharge was "anomaly of the intestine (intestinal band)."

On April 10, 1933, the patient entered the Los Angeles County Hospital again, complaining of dark stools, anemia and flatulence. The results of physical examination were essentially those previously described. The hemoglobin content was 17 per cent and the erythrocyte count 1.6 million; the urine was normal and the stools gave a strong reaction for occult blood. After improvement of her condition she was removed to a private hospital. A diagnosis of possible bleeding ulcer of the small bowel was made and exploratory laparotomy was performed on May 5. The antemesenteric band described at the previous operation and increased vascularity in the wall of the upper portion of the jejunum were noted. The cause of hemorrhage from the bowel was not found.

A diagnosis of vicarious menstruation from the bowel was next made by a private physician. Artificial menopause was produced by giving high voltage roentgen therapy over the ovaries. Within one week after the last of these treatments the patient had the most severe hemorrhage from the bowel she had yet experienced, Dec. 12, 1933. She was admitted to the Los Angeles County Hospital and the hemoglobin content was estimated as 8 per cent. Following transfusions, a high caloric diet and iron therapy, she recovered.

The next admission was on June 10, 1935. The complaints and manifestations were essentially those presented on previous entries. Hemoglobin was 26 per cent and the erythrocyte count 1.2 million. The usual treatment was given, she recovered and she was discharged with a diagnosis of endometriosis of the bowel and secondary anemia. This hospital experience was repeated in December 1938. The hemoglobin at this time was 8 per cent. The cause of hemorrhage had not been determined, although extensive studies had been made. Improvement followed the usual treatment but was followed two months later by another and more severe attack.

At this time a critical review of the entire situation was made. The principal features were more or less continuous hemorrhage from the bowel, severe exacerbations at frequent and irregular intervals and the presence of highly vascular sacculations in the walls of the upper portion of the jejunum, described at each of two exploratory laparotomies. In view of these facts the great mass of negative factors and the continued symptoms, it was suggested that a telangiectatic hemangioma of the jejunum would explain her symptoms and condition and would be in keeping with observations made concerning the jejunum at the two operations.

Laparotomy was again performed March 1, 1939. The increased vascularity of the jejunum was again observed. Telangiectases were present in the serosa of the jejunum and the proximal portion of the ileum. Three feet of small bowel extending from 1 foot distal to the origin of the jejunum downward was removed and an end to end anastomosis made.

Pathologic Examination.—The serosal surface of the specimen of bowel was very hyperemic. The mucosa was stained with bile and bright red blood but did not appear to be hyperemic or injected. No bleeding points or dilated vessels could be

seen on the mucosa. By microscopic examination of numerous sections of the jejunum, increased vascularity was seen in all layers. Large spaces lined with endothelial cells and containing blood were found in the serosa and muscularis. Occasional plexiform groups of small thin walled vessels were also present. An area of recent mucosal hemorrhage and a break in the continuity of the mucosal surface were found. The pathologic diagnosis was diffuse telangiectatic cavernous hemangioma of the jejunum.

Follow-Up Studies.—A record of monthly postoperative follow-up studies indicates that the patient has been free from symptoms and leading a normal life for a period of more than nine months.

COMMENT

A review of the literature indicates that benign tumors of the gastrointestinal tract are rare and that vascular tumors are especially rare in this group. Kornmann¹ states that hemangioma constitutes only 7 per cent of all benign tumors. From the surgical and autopsy material of the Johns Hopkins Hospital Geschickter and Keasbey² in 1935 reviewed the records of 570 patients who had been found to have tumors of the blood vessels. Of these, only ten were found to have hemangioma of the internal viscera including mesentery, kidneys and gastrointestinal tract.

Gascoyen³ in 1860 published the record of one patient who was found to have angiomatosis involving the parotid gland, skin, intestine and liver. The death of a patient as a result of a single massive hemorrhage from an ulcerated hemangioma of the duodenum was described by Laboulbène⁴ in 1872. Paci⁵ described in 1882 an extraordinary observation in which a patient evacuated spontaneously a large cavernous hemangioma and a large amount of blood following violent purging. The records of patients whose symptoms and signs were similar to those which accompany acute appendicitis were published by Shillito⁶ in 1921 and Landois⁷ in 1925. At operation these patients were found to have cavernous hemangiomas in the ileum a few inches from the ileocecal valve. Double intussusception at the site of a cavernous hemangioma was described by Nicoll⁸ in 1899. A rare condition in which the entire gastrointestinal tract was involved by multiple hemangiomas was described in 1910 by Winternitz and Boggs.⁹ The removal of a hemangioma from the duodenum after it had been located by x-ray examination was done by Judd and Rankin¹⁰ in 1922. A review of the literature by Brown¹¹ in 1924 indicated that hemangioma of the gastrointestinal tract, not including the stomach, had been reported in twenty cases. Brown classified gastrointestinal hemangioma as follows:

1. Multiple tumors of vascular arcades appearing as reddish nodules situated in the submucosa and connected with either an artery or a vein: (a) nevi, (b) cavernous hemangioma.

2. Submucous tumor which grows toward the lumen of the bowel and may ulcerate the overlying mucosa by pressure and trauma.

3. The submucosal hemangioma, which may grow to such a size that it may either obstruct the lumen of the bowel or cause a change in normal peristalsis, producing intussusception.

4. The diffuse, ringform hemangioma which begins in the submucosa involving the muscularis and constricts the lumen of intestine and is capable of producing intestinal obstruction.

McClure and Ellis¹² published in 1930 the records of twenty-five patients who had been found to have hemangioma of the gastrointestinal tract. Of these, fourteen were single and eleven multiple. The records of two additional patients and a complete review of the literature were published by Kaijser¹³ in 1936. He classified seventy-four verified instances of hemangioma of

1. Kornmann: *Zentralbl. f. Chir.*, 1913, p. 1427.
2. Geschickter, C. F., and Keasbey, L. E.: *Am. J. Cancer* 23: 568 (March) 1935.
3. Gascoyen: *Tr. Path. Soc. London* 11: 268, 1860.
4. Laboulbène: *Bull. Acad. de méd., Paris* 1: 462-464, 1872.
5. Paci, A.: *Sperimentale*, 49, 1882.
6. Shillito, M.: *Pennsylvania M. J.* 24: 421 (March) 1921.
7. Landois, F.: *Beitr. z. klin. Chir.* 133: 685, 1925.
8. Nicoll: *Brit. M. J.* 1: 842, 1899.
9. Winternitz, M. C., and Boggs, T. R.: *Bull. Johns Hopkins Hosp.* 21: 203, 1910.
10. Judd, E. S., and Rankin, F. W.: *Ann. Surg.* 76: 28 (July) 1922.
11. Brown, A. J.: *Surg., Gynec. & Obst.* 39: 191 (Aug.) 1924.
12. McClure, R. D., and Ellis, S. W.: *Am. J. Surg.* 10: 241 (Nov.) 1930.
13. Kaijser, R.: *Arch. f. klin. Chir.* 187: 351 (Nov.), 661 (Jan.) 1936.

the gastrointestinal tract into five groups, which may be summarized as in the accompanying table.

Kajiser's "hemangioma simplex" group is referred to by Ewing¹⁴ as being synonymous with "telangiectasis." Kajiser also included a fifth group in his classification, "hemangiomatosis." Cases under this classification present hemangiomas in other organs in addition to those found in the gastrointestinal tract.

The records of three patients who were found to have hemangiomas were published by Ackerman¹⁵ in 1937. One of these patients had multiple hemangiomas of the small intestine, large intestine and gallbladder. This patient died as a result of hemorrhage following perforation of the tumor retroperitoneally, which is extremely rare. A second patient presented a solitary hemangioma of the jejunum and a third presented multiple hemangiomas of the jejunum and ileum. Familial telangiectatic gastric and duodenal disease in a woman aged 62, verified at autopsy, was described by Schuster¹⁶ in 1937. She was found also to have telangiectasis in the skin, nose, mouth, pharynx, larynx and trachea. A report of two patients, members of the same family, suffering from massive gastric hemorrhages resulting from gastric telangiectatic bleeding, was published by Goldstein¹⁷ in 1937. Hemangioma involving all of the jejunum and part of the ileum was found by Peyton¹⁸ in 1938 at laparotomy on a youth aged 15. Buie and Nesselrod¹⁹ reported

Kajiser's Classification of Verified Instances of Hemangioma of Gastrointestinal Tract

Classification (Kajiser)	Pinpoint Multiple Varicos- ities	Diffuse Infil- trating Cavern- ous Heman- gioma	Circum- scribed Cavern- ous Polypoid Heman- gioma	Heman- gioma Simplex (Telan- giectasis)	Heman- gioma- tosis
Group.....	I	II	III	IV	V
Sex.....	24 M; 3 F	14 M; 8 F	5 M; 5 F	5 M; 2 F	2 M; 5 F; 1 ?
Age variation.....	26-70	3 mo.- 48 yr.	15-62	3 mo.- 64 yr.	2 mo.- 61 yr.
Location:					
Esophagus.....	2	1
Stomach.....	2	2	2
Duodenum.....	2	..
Jejunum.....	9	1	..
Ileum.....	7	1	..
Meckel's diverticulum.....	1
"Small intestine".....	..	7	4	1	3
Cecum.....	1	1
Sigmoid flexure.....	..	7	1
Rectum.....	3	12	3
"Large intestine".....	9	2
"Gastrointestinal tract".....	1	..	6
Total cases.....	27	22	10	7	8

a case in 1938 in which diffuse cavernous hemangiomas of the rectum and right renal pelvis occurred. The patient, a man aged 28, died as a result of multiple hemorrhages from the rectum. Successful surgical treatment of a patient who had hemangioma of the sigmoid was recorded by Bancroft²⁰ in 1931. After a colostomy was performed, the superior hemorrhoidal vein was ligated and then injected with 10 cc. of 40 per cent sodium salicylate. Exploratory laparotomy, closure of the colonic stoma, cecostomy and appendectomy were done on this patient eleven months after the original operation.

SUMMARY AND CONCLUSION

A patient who suffered from telangiectatic cavernous hemangioma involving the jejunum and upper ileum underwent surgical removal of the hemangiomatous portion of the intestine, which greatly improved her condition.

When a patient experiences repeated attacks of melena which cannot be explained by a thorough study of the history, physical manifestations and laboratory examinations, the possibility of hemangioma of the gastrointestinal tract should always be considered.

14. Ewing, James: *Neoplastic Diseases*, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 241.
15. Ackerman, L. V.: *Am. J. Cancer* 30: 753-757 (Aug.) 1937.
16. Schuster, N. H.: *J. Path. & Bact.* 44: 29-39 (Jan.) 1937.
17. Goldstein, H. L.: *M. Rec.* 146: 530-533 (Dec.) 1937.
18. Peyton, William: *Minnesota Med.* 21: 590-593 (Aug.) 1938.
19. Buie, L. A., and Nesselrod, J. P.: *Surgery* 3: 379 (March) 1938.
20. Bancroft, F. W.: *Ann. Surg.* 94: 828-838 (Nov.) 1931.

Special Article

CONFERENCES ON THERAPY

TREATMENT OF BLOOD DISORDERS

VIII. HEMORRHAGIC DISEASES

NOTE.—These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments and institutions. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Treatment of Blood Disorders: IX. Management of Polycythemia and Hodgkin's Disease."

DR. CLAUDE E. FORKNER: Today we take up hemorrhagic diseases; the first part of the program will deal especially with hemophilia. Dr. Patek, formerly of the Thorndike Laboratory in Boston and now with the Research Division of Welfare Island Hospital, will talk about the therapeutic aspects of hemophilia.

THERAPEUTIC ASPECTS OF HEMOPHILIA

DR. ARTHUR J. PATEK JR.: The measures advocated for the treatment of hemophilia may be separated, for the sake of convenience, into two general groups. The first may be classified as empirical therapy, the second as rational therapy. The first group includes measures that have been tried because they were shown to be effective in other conditions that resemble hemophilia in certain aspects of their symptomatology. Unfortunately not one of these procedures is of established value. They include the administration of vitamin concentrates, calcium salts, extracts from liver, lung, placenta and bone marrow, and numerous other preparations.

The rational therapy for hemophilia or, indeed, for any disorder depends on an understanding of the etiology and of the pathologic physiology of the disease. Obviously the etiology of hemophilia is related to an inborn fault. Since hemophilia is sex linked, it was supposed that the disease might be related to an endocrine defect. With this in mind Birch and others administered ovarian substance and female sex hormones to patients with hemophilia. Subsequent trial of this therapy by others has been disappointing. Moreover there was little, if any, evidence that patients with hemophilia lacked estrogenic substances. Nevertheless it may well be that there is a regulator for the clotting mechanism which in some manner is related to the sex hormones. The regulation of salt metabolism by the adrenal cortex might serve as an analogy.

In recent years attention has been directed to the blood clotting mechanism itself, which appears to be the immediate locus of difficulty. The various studies of this problem agree that the clotting of hemophilic blood is retarded. The retardation of clotting appears to take place in the first phase, or in the conversion of prothrombin to thrombin. There are differences of opinion concerning the fault at this point. Some investigators attribute the delay to a qualitative change in prothrombin, others to the lack of available thromboplastin, still others to the lack of an unknown substance which is present in normal plasma and which may be precipitated with the globulin fraction of the plasma. Certain workers incriminate the blood platelets in the problem, while others believe that the clotting defect bears no essential relation to the blood platelets. From the point of view of treatment these differences of opinion are of no immediate concern. However, from

these various studies several practical measures for the treatment of hemophilia have evolved.

These measures are based on the observation that transfusion with normal blood shortens the hemophilic clotting time. The maximal effect from transfusion is almost immediate. In the course of from eighteen to forty-eight hours there is a gradual return of the clotting time to its original, abnormal value. The transfusion with 100 cc. of blood is as effective as the transfusion with 500 cc. Therefore, unless the patient urgently needs hemoglobin, a transfusion of 100 cc. of blood at twelve hour intervals is preferable to a transfusion of 600 cc. at three day intervals.

Transfusion of normal citrated plasma is also effective in reducing the clotting time of hemophilic blood. There are certain advantages to its use. It may be stored for weeks in the ice box without appreciable change. It may be administered without regard to blood groups. In my experience, at least, no untoward reactions have followed the repeated administration of 100 cc. of pooled plasma. When using plasma for this purpose it is advisable to take the precaution of passing it through the Berkefeld filter to remove particulate matter.

In the treatment of superficial bleeding, as from the nose or tooth sockets, the local application of certain tissue extracts and of blood derivatives has been shown to be of help. Perhaps the most potent of these are the dried "globulin substance" and dried thrombin. These substances are stable in dried form. They are obtainable from animal sources. If these are applied in powdered form to the surface of moistened gauze and packed against the bleeding point, they are usually effective. A dry or powdered preparation is preferable to a liquid because it is not washed away so readily by the oozing blood.

There are several clinical features of the disease that I should like to stress, since they are not usually emphasized. The first of these relates to intercurrent infections. It is very common to observe bleeding episodes occurring either with infection or several days after the onset of infection. Indeed, the bleeding point may bear a relation to the site of infection, such as epistaxis with rhinitis, or retropharyngeal bleeding with pharyngitis, or bleeding gums with abscessed teeth. It is sometimes said that hemophilia is milder in summer than in winter. This seasonal variation in hemophilia more probably is related to the upper respiratory infections in winter.

The commonest complication of hemophilia is hemarthrosis. When this occurs, small transfusions should be given for several days to prevent further bleeding. The joints become swollen, tender and painful. If bleeding extends into the tissues about the joint, the overlying skin becomes warm and discolored. Pain and discomfort are alleviated by the administration of salicylates and by immobilization of the joints in cotton wool swaths or loose splints. After the acute symptoms subside, gentle massage, radiant heat and active motion may be tried. In my opinion the ankyloses and deformities resulting from hemarthroses are due in part to the premature resumption of joint motion.

Surgical emergencies present the most difficult decisions. Hemorrhage in the submucosa of the posterior pharynx, in the body of the tongue or in the tissues of the neck may all but strangle these patients. However, counterpressure from the distended tissues generally checks the bleeding in these areas. In such instances it is best to give transfusions and to avoid

surgical intervention. Bleeding into the abdominal wall or cavity may simulate peritonitis or appendicitis. Bleeding in the urinary tract may produce renal or ureteral colic. Here too treatment should be palliative. Indeed, the simplest and safest rule to follow is to avoid surgical procedure unless it is unavoidable. Under such circumstances it is essential to prepare the patient by transfusions both preoperatively and postoperatively. Although I have never seen it applied, the transfusion by means of the continuous drip method should be ideal for such emergencies. The operative risk in hemophilia is enormous.

THROMBOCYTOPENIC PURPURA

DR. FORKNER: Before we discuss Dr. Patek's contribution I think we will ask Dr. Reznikoff to talk about thrombocytopenic purpura.

DR. PAUL REZNIKOFF: Thrombocytopenic purpura ought to be discussed by the surgeon because treatment is, for the most part, surgical. Many suggestions have been made regarding nonsurgical methods of treatment. For a time vitamin C was given in large amounts, but I am sure that all workers agree that in typical thrombocytopenic purpura vitamin C is valueless. Then Dr. Mettier tried roentgen therapy of the spleen, and, while he feels that he has seen some temporary improvement, most workers who have tried it have not substantiated these results and are not enthusiastic about irradiation of the spleen. Of course, watchful waiting and transfusions have been used in many cases. We hesitate to operate on a patient who is bleeding profusely and who is not a good surgical risk. I believe that one patient who was operated on here had a red cell count of less than a million, and that is not a happy prospect for the surgeon. In such cases transfusions are given, and many reports tend to show that multiple transfusions will tide a patient over the acute phase of the disease and put him in condition for operation. However, it is difficult to evaluate these cases since we know that many patients with thrombocytopenic purpura have spontaneous remissions, and good controls are difficult to obtain. My own feeling in the matter is that there is only one treatment for thrombocytopenic purpura, and that is splenectomy. Why this should be effective we don't know. Troland and Lee thought they could demonstrate a platelet depressing agent in the spleens removed from patients with thrombocytopenic purpura, but I do not think that has been substantiated. Meyer and Pohle, of Wisconsin, could not confirm these observations, and it is impossible to say whether the disease is due to faulty formation of platelets or to increased destruction. We certainly find in the bone marrow of these patients pictures of both sorts, in some an apparent increase of megakaryocytes and in others a marked decrease.

As far as operation is concerned, the most important thing is the choice of the surgeon. Here we have operated on fourteen or fifteen patients with thrombocytopenic purpura when we were sure of the diagnosis and thus far we have had no deaths. When the surgeon clamps off the pedicle of the spleen something happens; it is striking to see all the oozing stop within less than a minute. This treatment is safe if the procedure is carried out rapidly and transfusions are available. Excellent results are being obtained in other centers. It would seem wiser to operate early in these cases than to pursue a policy of watchful waiting and run the danger of a death from cerebral or other hemorrhage.

Our experience shows that some patients do not retain the high platelet count that they have just after the operation. We have had some patients with platelet counts that are down to 30,000 again, but I do not think any of them have had a recurrence of bleeding. It has been reported in some series that 30 per cent of these patients have recurrence of thrombocytopenic purpura, and many of them subsequently die. We have not seen that in our cases.

THERAPEUTIC ASPECTS OF HEMORRHAGIC DISEASES IN INFANCY AND CHILDHOOD

DR. FORKNER: Dr. Schloss, will you discuss the therapeutic aspects of hemorrhagic diseases in infancy and childhood?

DR. OSCAR M. SCHLOSS: Practically the only hemorrhagic condition peculiar to early life is the so-called hemorrhagic disease of the newborn.

During the first few days of life, usually from the second to the fifth, the newborn infant may develop spontaneous hemorrhage. There is great irregularity in the source of the bleeding and its severity. It may originate in the skin, subcutaneous tissues, viscera, serous membranes or cranial cavity. Often the degree of hemorrhage is slight and the bleeding may cease spontaneously within a short time. At the other extreme, death from exsanguination may occur within a few hours.

Up to now no definite or uniform cause of hemorrhage in the newborn has been established. Many investigations of the platelet count, bleeding time, clotting time and other factors involved in hemorrhagic disease have given inconstant results. Occasional cases have been observed in which there was a thrombocytopenic picture or in which blood clotting was greatly delayed, but often all such investigations have thrown no light on the cause of hemorrhage.

The best treatment is the administration of human blood. Whole blood may be given by intramuscular injection, but unquestionably transfusion is the method of choice. Transfusions of about 10 cc. of blood per kilogram of body weight are usually adequate and may be repeated in from one to three days if indicated.

Transfusions serve two purposes: (1) the replacement of lost blood and (2) the relief of the tendency to bleed. Citrated blood always fulfils the first requirement and usually both, but occasionally it is necessary to give unmodified blood by direct transfusion to control the bleeding tendency effectively.

Within the last few years, evidence has accumulated which indicates that vitamin K deficiency may be a factor in some cases of spontaneous hemorrhage in the newborn. It has been noted by Owen, Hoffman, Ziffert and Smith, Hellman and Shettles, Moore and Javert and others that in the newborn prothrombin has only from 14 to 39 per cent of the values found in adults. More important are the observations that the prothrombin falls to an even lower level sometime between the second and seventh days of life, the period during which hemorrhage is most apt to occur. Thus far, a few cases have been reported by Quick, Dam, Waddell and Guerry and others in which abnormally low prothrombin of bleeding infants was raised to normal by the administration of vitamin K, with coincident cessation of bleeding. Much further evidence is necessary to clarify the possible relationship of vitamin K deficiency to hemorrhagic disease in the newborn. Such evidence should be forthcoming soon, as the subject is being actively investigated in a number of clinics.

If it is demonstrated that vitamin K deficiency is the usual or even a common cause of bleeding in the newborn, prophylactic treatment will probably become universal. Hellman and Shettles have shown that the administration of large doses of vitamin K to the mother, even shortly before the infant is born, can raise the infants' prothrombin to three times the average value.

Meanwhile the administration of vitamin K or an effective chemical substitute (2-methyl-1,4-naphthoquinone) in addition to blood transfusions would seem a rational procedure. It would naturally be best to do this under the guidance of prothrombin time determinations, but even if this is not possible vitamin K may be given empirically in all cases of severe or persistent hemorrhage.

VITAMIN K

DR. FORKNER: I think that it might be well now, as the subject of vitamin K has been brought up and is so important, to ask Dr. Andrus and Dr. Chambers to say a few words about their work with it. We would like to hear from Dr. Andrus with regard to the control of hemorrhage in surgical conditions by means of vitamin K, and something about the chemistry and physiology of vitamin K from Dr. Chambers.

DR. WILLIAM DEW. ANDRUS: The conditions for which we use vitamin K therapy in surgery are particularly the hemorrhagic tendency in jaundice and the similar tendency which may occur in the presence of severe liver disease. I think it is now pretty well accepted that any patient with a plasma prothrombin level below 60 points on the Smith scale or 70 points by the Quick test should receive vitamin K. Prothrombin deficiencies are much more widespread than one would think but usually are not of such severity as to be critical. However, after surgical operations and after hemorrhage the body and compensatory mechanism for maintaining blood volume may dilute the prothrombin to a critical point. We have evidence that in patients who, because of gastric ulcer or carcinoma, have been on a markedly deficient diet before operation, the operation itself may depress the prothrombin still further, and this plus an inadequate vitamin intake following the operation may cause the prothrombin level to fall below the point at which hemorrhage occurs.

As far as the actual therapy is concerned, several methods can be used. Vitamin K can be given by mouth with bile salts if the latter are not present in the gastrointestinal tract, but I think that the method which will come to be used from now on is the administration either by mouth with bile salts, if necessary, or hypodermically of synthetic naphthoquinone derivatives, either the 2-methyl-1,4-naphthoquinone of Ansbacher or the compound which Fieser has brought out, which contains a phytyl group in addition. This substance is tremendously potent so far as its prothrombin forming activity is concerned. We have patients in whom the injection of 1 mg. of 2-methyl-1,4-naphthoquinone has elevated the plasma prothrombin by 50 points and has maintained it at a high level for a period of several days. In a newborn child 0.5 mg. produces a corresponding rise. One mg. in a dog will elevate the plasma prothrombin level as much as 50 points and keep it elevated for two weeks. Furthermore, there is a wide gap between the therapeutic and the toxic dose of this material. It requires something on the order of 2 mg. per kilogram to produce toxic effects in animals, and a total dose of 1 mg. a day in an adult is entirely adequate. The substance can be injected in corn oil for

slow absorption, or the dipropionate can be injected in twice the amount, that is 2 mg. subcutaneously. We have done microscopic studies in animals of the muscle into which injections of these substances have been given and we find no untoward reaction. A very comforting point is the fact that no matter how much vitamin K is given subcutaneously, orally or even intravenously, the prothrombin can never be forced above 100 per cent of normal by that method alone.

DR. FORKNER: Dr. Chambers, may we have a word about the chemistry of vitamin K?

DR. WILLIAM H. CHAMBERS: Vitamin K was first prepared in highly purified form as a yellow oil extracted from alfalfa or other green plant materials. Work on purification of crystalline material progressed very rapidly in several laboratories early in 1939. In the July issue of the *Journal of the American Chemical Society* four laboratories agreed essentially on a naphthoquinone structure with a phytyl (C_{20}) side chain. The four groups are Almquist and Klose; Doisy, Thayer, MacCorquodale and their co-workers; Riegel, Fieser and their co-workers, and Ansbacher and Fernholz. Recent synthesis has shown that the chemical structure of vitamin K_1 derived from alfalfa is a 2-methyl-3-phytyl-1,4-naphthoquinone. The phytyl group is not necessary for the antihemorrhagic activity.

Decomposed fish meal yields a substance with a somewhat different structure, which has been labeled vitamin K_2 by the St. Louis group.

DR. FORKNER: Will you tell us something of the relationship of vitamin K to liver function?

DR. CHAMBERS: The low prothrombin content of the blood in vitamin K deficiency may be due to several causes, as outlined by Snell and Butt in recent Council reports published in *THE JOURNAL*. In the test chicken and other animals the avitaminosis is produced by a vitamin K deficient diet. This condition may also be found clinically. Since it is a lipoid material, absorption of the vitamin is helped by bile salts. The jaundiced patient suffers from lack of adequate absorption.

The fall in blood prothrombin after liver damage by chloroform or partial or complete hepatectomy points to the liver as the source of prothrombin. Some cases with severe liver damage have been reported which would not respond to vitamin K therapy.

PARENTERAL USE OF THE GLOBULIN FRACTION

DR. REZNIKOFF: I should like to ask Dr. Patek whether he would tell us something about the present status of the globulin fraction in the treatment of hemophilia, that is, the parenteral use of the globulin fraction.

DR. PATEK: The term globulin fraction, or substance, of necessity is vague because its chemical nature is not yet known. It simply means that the material effective for the clotting of hemophilic blood is obtained from normal plasma with the globulin fraction. It has been shown that the effective substance is neither prothrombin nor fibrinogen. In the treatment of hemophilia I see no advantage in the use of globulin substance over transfusion with blood, because the material is derived from human blood and there must obviously be some loss in its preparation. If a store of the dried powder were available, and if no transfusion were within reach, I think it would be serviceable for an emergency.

In the earlier studies with Dr. Taylor, I found that a clot accelerating substance was obtained either by

dialysis or by acid precipitation of diluted plasma. We used the latter method for subsequent studies because it was easier to prepare. Unfortunately we assumed the substances obtained by either method to be the same. Later, Pohle and Taylor demonstrated that a refractory phase developed in the response of the hemophilic to globulin substance when injections were repeated at frequent intervals, say six hours apart, but that this did not happen when the injections were spaced at twenty-four hour intervals. What takes place in the acid precipitation method to bring about this effect I don't know. I wish that you could help explain it. However, recently Lozner and Taylor showed that the refractory phase did not occur when the injected material was prepared by the method of dialysis. In other words, globulin substance prepared in this manner behaves in its clot accelerating power like the parent plasma.

DR. HARRY GOLD: Is it possible to say that blood given intramuscularly is not as effective as a transfusion for the control of hemorrhage in hemophilia?

DR. PATEK: I have not had experience enough to say. It causes considerable discomfort. I suppose that you could give 30 or 40 cc. intragluteally by injecting 15 or 20 cc. in each buttock, but you could not do it repeatedly and have a grateful patient.

DR. FORKNER: The question of intramuscular injection of blood comes up occasionally, as with a patient who has a very severe hemorrhage for whom there is not time to prepare for a transfusion, and one wonders whether or not an injection of 15 or 20 cc. of blood might not control a hemorrhage. I think it is a good thing to do. It might occasionally save the patient's life, and of course one does not have to group the blood before making an intramuscular injection. Anybody's blood would be all right.

DR. GOLD: Are any of the tissue extracts on the market that are recommended for intravenous or systemic administration for the control of hemorrhage of any value in the bleeding of hemophilia, such as Tissue Fibrinogen of Merrell? They were at one time exploited actively, and some outstanding men at that time seemed to think that our problems were over. All we had to do was to give a dose of tissue fibrinogen intravenously, and lo and behold!

DR. PATEK: I have not used those either, so I am not qualified to say. I think the fact that they have not survived in popular use is evidence against them. The most promising of those measures has been the placental extract of Eley and his associates, which in certain instances undoubtedly was effective. However, results with this preparation have been inconstant. It may be that with refinement either in the method of preparation or in the mode of administration this may prove to be useful. It is based on the same principle as the lung extracts of Mills and others that you mentioned.

DR. FORKNER: With regard to tissue extracts of various sorts, and I think Dr. Reznikoff will agree with me, almost all of those which have heretofore been prepared for commercial sale are practically useless in the control of thrombocytopenic purpura, hemorrhagic disease of the newborn or hemophilia.

DISCUSSION OF QUESTIONS

STUDENT: How long does the effect of a transfusion last in a case of hemophilia?

DR. PATEK: It is a question of what you mean by effect. The clinical effect, as far as the arrest of bleed-

ing is concerned, may last twelve hours or so. It is variable from patient to patient. To illustrate with a specific example, let us suppose that the initial clotting time of a patient is 150 minutes. After transfusion the clotting time may be reduced abruptly to eight minutes. In the course of twelve hours the clotting time may increase to twenty-five or thirty minutes, which may be the level or threshold at which bleeding occurs in this case. In the subsequent twelve or twenty-four hours the clotting time may return to the original value of 150 minutes.

DR. FORKNER: Dr. Patek, you mentioned transfusion of 100 cc. of blood being as effective in inducing an immediate result as 500 cc. Could one carry that still further and say that 10 cc. of normal blood will be as effective?

DR. PATEK: I have not quantitated it to that extent; 30 and 40 cc. was as effective in my hands as 500 cc.

DR. REZNIKOFF: It is rather surprising that nobody in discussing hemorrhagic states so far has mentioned any of the snake venoms. I wonder if anybody would like to tell us the status of those products.

DR. FORKNER: Would anybody like to discuss snake venoms? Will you say a word about them, Dr. Reznikoff?

DR. REZNIKOFF: I think there is little to be said in their favor. The only experience we have had has been with moccasin venom and the so-called fer-de-lance. Moccasin venom has given us no results at all, but the fer-de-lance has given us results when applied locally. For instance, with bleeding gums in acute leukemia or uremia, if we apply it locally in some cases we apparently do stop the bleeding. We had one patient who had capillary hemorrhages and bled profusely postoperatively. We sprayed the fer-de-lance preparation and the bleeding stopped.

DR. FORKNER: I think many mistaken reports which have appeared about the effectiveness of various agents in hemophilia and hemorrhagic disease have their source in an inadequate knowledge of the natural history of the disease. Frequently it happens that when a patient bleeds he tends to control his own hemorrhage; and the hemophilic patient who bleeds, whether into his own tissues or externally, is apt to lower his own coagulation time so that any therapeutic agent given at that time will tend to make one think that he is obtaining a therapeutic effect.

VISITOR: It should be borne in mind that the use of certain drugs, for example quinine, may cause acute thrombocytopenic purpura. In these cases it is only necessary to stop their use to stop the bleeding and cure the purpura.

DR. FORKNER: I think the point which has just been brought out should be emphasized. We are trying to remove the cause, where possible, of the various disorders. One frequently thinks of treating the disease without attention to the cause, when it is apparent that, particularly in thrombocytopenic purpura, it is the cause that must be removed.

DR. GOLD: I am struck by the difference in the opinions regarding snake venom in two institutions that are removed from each other by only a few blocks. Since 1931 several papers have appeared on the use of snake venom or moccasin venom in the treatment of various types of hemorrhage. Its introduction for the treatment of thrombocytopenic purpura was based on the interesting observation that snake venom prevents the Shwartzman reaction, which suggested an

increased resistance of the small blood vessels. It has been tried in various types of hemorrhage, in thrombocytopenic purpura, in ordinary uterine hemorrhage and in others of that sort. Reports indicate improvement in a large proportion of cases treated. But here we are; we learn that the experience in this institution fails to confirm it. This seems to be the way with agents introduced for the control of hemorrhage.

DR. McKEEN CATTELL: I should like to go back to vitamin K and ask what the group here thinks about Quick's suggestion that hemorrhagic disease in infancy may be related to the failure of the digestive processes to provide vitamin K until after the bacterial flora has been developed.

DR. SCHLOSS: Quick observed that the prothrombin of newborn infants fell from the second to the sixth day and then rose to normal. He suggested that this secondary rise was caused by the production of vitamin K by the bacteria of the intestinal tract.

DR. ANDRUS: Ordinarily the prothrombin content of a child's blood does not reach adult values until the age of 6 months or the end of the first year, although I think the flora of the stool begins to form before that time, does it not?

DR. SCHLOSS: It begins to form as soon as food is taken. What actually happens is that the secondary rise brings the prothrombin to the previous newborn level, which is about 30 per cent of the normal adult level as determined by most methods in use at present. By Quick's method, however, blood of the newborn infant contains practically as much prothrombin as blood of the adult.

STUDENT: I understand that in one clinic intramuscular injections of the patient's own blood are given; i. e., they draw it from the vein and reinject it.

DR. FORKNER: In hemophilia?

STUDENT: Not only in hemophilia; I heard of a case of bleeding due to uremia in which that was done, but I am not clear why.

DR. FORKNER: I think the explanation for that is that an intramuscular injection of blood may act in much the same way as a hemorrhage does, in that the individual interprets it as a hemorrhage and mobilizes his forces against it and in that way reduces his own coagulation time. Have you anything to say about that, Dr. Reznikoff?

DR. REZNIKOFF: There exists the possibility that in the blood clot there is formed a degradation product similar to the substance which Dr. Patek discussed.

DR. GOLD: Is there any experience with parathyroid extract in the treatment of hemophilia?

DR. PATEK: I don't know of any. Calcium salts of course have been tried.

DR. CHARLES O. WARREN: In what type of jaundice is vitamin K treatment indicated? Can you tell without determining the prothrombin value in the blood?

DR. ANDRUS: No, you cannot tell, for it depends on several factors. Of course, in hemolytic jaundice it is not indicated at all. It is indicated for vitamin K starvation, inadequate vitamin K absorption or inability on the part of the liver to form prothrombin. We now have the cycle of prothrombin pretty well worked out. It is influenced in its formation by vitamin K. Whether the vitamin K as such is actually the precursor or not is a question, but prothrombin is apparently formed continuously in the liver, and by inference only in the liver, because if one performs complete hepatectomy in

a dog one gets a drop of 50 per cent in the plasma prothrombin level in the first three hours and then a gradual fall to practically 0 in fourteen hours. This is not caused by shock and is not caused by operations of similar magnitude. Further, the curve of fall in the plasma prothrombin level after hepatectomy is not altered by the availability of even massive quantities of vitamin K at the time of operation. The mere availability of the vitamin will not elevate the plasma prothrombin if the liver function is seriously deranged.

In looking for differences in prothrombin content between arterial and venous blood, we find there is an average of 11 per cent and extremes of from 4 to 19 per cent difference between the blood in the right and in the left side of the heart. The incidence and extent of this difference correspond exactly to the difference in the platelet counts in the heart's blood of the right and left sides as shown by Howell and Donahue. The cycle of prothrombin would therefore seem to be that it is formed in the liver under the influence at least of vitamin K, or of the naphtha quinone group, being continuously formed here and apparently only there because it falls so rapidly after hepatectomy. It is destroyed at the rate of about twice the total circulating prothrombin every twenty-four hours, and this destruction or neutralization takes place possibly through the thromboplastic activity of the platelets and therefore appears most markedly in the pulmonary veins, where the platelet count is materially above what it is elsewhere.

SUMMARY

DR. FORKNER: The exact mechanism of the cause of bleeding in hemophilia is still unknown. The prolonged clotting time is restored to and maintained at normal values by repeated transfusions of 50 or 100 cc. of blood. For the control of bleeding in accessible parts the local application of "globulin substance," preferably in powdered form, may be effective. Bleeding into joints may be treated by limitation of activity, by salicylates and by transfusions of blood. Patients with hemophilia should lead a guarded life. Potential carriers of hemophilia should not reproduce.

Splenectomy preceded and followed by transfusions of blood produces dramatic and usually permanent cessation of the bleeding tendency in acute or chronic idiopathic thrombocytopenic purpura.

Hemorrhagic disease of the newborn may be associated with decreased prothrombin content of the blood. Evidence is accumulating that administration of vitamin K to the infant or even to the pregnant mother will overcome this defect. At present this disease is best treated by transfusion of 10 cc. of blood per kilogram of body weight repeated after two or three days.

The hemorrhagic tendency associated with some types of jaundice has been shown to be related to decreased prothrombin in the blood. This decrease may be due to inability of the liver to form prothrombin or deficiency of vitamin K. In the absence of bile salts the absorption of this vitamin is greatly inhibited. The administration by mouth of vitamin K or of 2 methyl 1-4 naphthoquinone together with bile salts restores the prothrombin and causes bleeding to cease. The 2 methyl 1-4 naphthoquinone may be effectively administered parenterally in doses of 1 mg. daily. Such medication should be guided by repeated observations of the prothrombin content of the blood.

Sufficient time was not available to discuss non-thrombocytopenic purpura and the bleeding tendency in leukemia and erythremia and in other rarer disorders.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.
HOWARD A. CARTER, Secretary.

ACOUSTICON HEARING AIDS GOLD MEDAL MODELS ACCEPTABLE

Manufacturer: Dictograph Products Company, Inc., 580 Fifth Avenue, New York.

The Acousticon, Gold Medal Models, GM-1 and GM-2, are wearable hearing aids adaptable to use with bone or air conduction. The Council's report is based on investigation of the following:

- One GM-1 Microphone serial number 4357, weight 58 Gm.
- One GM-2 Microphone serial number 03486, weight 81 Gm.
- One number 1 Midget air conduction receiver with right and left ear pieces, weight 11.5 Gm.
- Two S-2 Gm. amplifiers.
- One "One dot" bone conduction receiver, weight 18 Gm.
- One number 9 3 volt dry battery, weight 250 Gm.
- One number 6 4½ volt dry battery, weight 187 Gm.

Battery Consumption.—The current drains of the various combinations are:

- GM-1 Microphone, any receiver, 3 volt battery, 35-55 milliamperes.
- GM-1 Microphone, any receiver, 4½ volt battery, 55-120 milliamperes.
- GM-2 Microphone, any receiver, 3 volt battery, 20-55 milliamperes.
- GM-2 Microphone, any receiver, 4½ volts, 60-100 milliamperes.

Internal Noise.—The internal noise in this instrument under conditions of use, or with the microphone attached to the clothing of the wearer, is of the order of 20 decibels above the normal threshold. With the microphone turned full on there is a tendency for the instrument to feed back with the air conduction receiver, thus limiting the range of full amplification. With the number 1 receiver and fitted ear piece the microphone may be used up to about three-fourths full volume without feed back difficulties. There is no feed back difficulty with any combination using the bone conduction receiver.



Acousticon Hearing Aids, Gold Medal Model.

Amplification.—All the combinations tried show enhanced amplification in the range of 1,000 to 2,000 cycles. The results in table 1 are fairly typical of measurements made with two hard of hearing subjects.

TABLE 1.—Amplification

Microphone	Receiver	Battery	Amplification in Decibels					
			123	256	512	1,024	2,048	4,096
GM-1	#1	#3 4½ volts	4	4	10	22	24	None

Articulation Tests.—Typical of the best results of articulation tests made with various combinations using hard of hearing subjects and standard articulation tests are those given in table 2.

TABLE 2.—Articulation

Microphone	Receiver	Battery	Syllable Articulation Per Cent	Sentence Intelligibility Per Cent
GM-1	#1	#3 (3 volts)	64	83
GM-2	Bone	#6 (4½ volts)	68	90

The instrument is pleasing in appearance and all parts are mechanically well made.

The Council on Physical Therapy voted to accept the Acousticon Hearing Aids, Gold Medal Models, GM-1 and GM-2, for inclusion on its list of accepted devices.

**DeVILBISS SPRAYERS, ATOMIZERS,
VAPORIZERS ACCEPTABLE**

Manufacturer: The DeVilbiss Company, Toledo, Ohio.

The following DeVilbiss devices have been investigated by the Council:

Atlas No. 32 powder blower. Of three-piece glass and metal construction; economically fabricated. The glass bottle, when one-half full, contained 25 cc. Eighty mesh powder consisting of equal parts of aluminum oxide and silicic acid was carried 10 inches from the nozzle and spread through an angle of 15 degrees.

DeVilbiss No. 288 powder blower. Consists of a hard rubber nozzle, tube and 30 cc. glass bottle. Ejects a powerful stream of 80 mesh powder for a distance of 15 inches through an angle of 25 degrees.

DeVilbiss No. 252 powder blower. Consists of a hard rubber nozzle and 15 cc. glass bottle with rubber bulb. Eighty mesh powder was ejected over an angle of 25 degrees for 15 inches.

DeVilbiss No. 260 atomizer for tannic acid. Consists of a metal cap with short nozzle, rubber bulb and glass bottle marked for 75 cc. of 10 per cent acid and water sufficient to make 160 cc. A small volume of water, in large globules, was injected over an area 3 inches in diameter from a distance of 10 inches.

DeVilbiss No. 177 syringe. Pressure instrument, with release vent, consisting of a 150 cc. glass bottle and long, slim metal nozzle ejecting a continuous fine stream of liquid.

DeVilbiss No. 286 power atomizer. Consists of hard rubber nozzle and tube with a 30 cc. glass bottle. The large volume of aqueous spray consisted of mixed large and small globules, concentrated toward the center; at 5 inches an area 2 inches in diameter was covered and at 10 inches a 3½ inch diameter was covered.

DeVilbiss No. 287 power atomizer. Similar to No. 286 except that there was an upturned extension on the nozzle. The spray contained both fine and coarse droplets and covered a 2 inch area at 5 inches distance and 3½ inches at 10 inches.

DeVilbiss No. 151 power atomizer. Consists of a long, slim metal nozzle and glass bottle of 30 cc. capacity. A small volume of, very fine evenly distributed spray was ejected. At a distance of 5 inches an area 1½ inches in diameter was covered, and at 10 inches a 2 inch diameter was covered.

DeVilbiss No. 43 glass nebulizer. A one-piece 10 drop size instrument of glass with a rubber bulb. It yielded a very fine mist which carried for 6 inches.

DeVilbiss No. 40 glass nebulizer. A one-piece, 20 drop size instrument of glass with a rubber bulb. It yielded a very fine mist which carried for 4 or 6 inches as determined by an opening in the bulb which regulated the air intake.

DeVilbiss No. 12 adjustable tip atomizer. Consists of an adjustable metal nozzle, 15 cc. bottle and rubber bulb. The spray was fine and small in volume, covering an area 3 inches in diameter at 5 inches and 5 inches in diameter at 10 inches.

DeVilbiss No. 19 adjustable tip atomizer. Consists of a rotating, self-closing metal nozzle, 15 cc. glass bottle and attached rubber bulb. The fine aqueous spray covered an area 3 inches in diameter at 5 inches distance and 5 inches in diameter at 10 inches. Using liquid petrolatum, the spray covered an area 2½ inches in diameter at 5 inches distance.

DeVilbiss No. 27 adjustable tip atomizer. Consists of a metal nozzle with attached rubber bulb and 15 cc. glass bottle. The aqueous and oily sprays were similar to those from No. 19.

DeVilbiss No. 251 hard rubber atomizer. Consists of a hard rubber nozzle, rubber bulb and 15 cc. glass bottle. A large amount of an aqueous medium was ejected in varying sized droplets. The area covered by the spray at 5 inches distance was 2 inches in diameter and at 10 inches was 3½ inches.

DeVilbiss No. 170 surgeon's atomizer. Intended for alcoholic solutions and consisted of a long metal nozzle and 185 cc. glass bottle. It yielded a fine, dense spray which covered an area 3 inches in diameter at 5 inches distance and 5 inches in diameter at 10 inches.

Atlas No. 112 electric steam vaporizer. Operates on the principle that steam generated by a submerged electric heater, when passed over cotton containing a volatile oil, will carry off some of the oil. It consisted of a 200 cc. glass jar in a metal frame

covered by a metal cap to which was attached a fire clay-enclosed heating element and spout. The metal parts were found to rust easily. The heating element took thirty minutes to raise the temperature of 120 cc. of water from 25 C. to 100 C. After boiling started, steam was steadily generated.

The Council voted to accept the DeVilbiss Devices Nos. 12, 19, 27, 32, 40, 43, 112, 151, 170, 177, 251, 252, 260, 286, 287 and 288 for inclusion on its list of accepted devices.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.
PAUL NICHOLAS LEECH, Secretary.

**RESYL-CIBA NOT ACCEPTABLE
FOR N. N. R.**

Resyl-Ciba is a guaiacol compound claimed to be glyceroguaiacol-ether which has been extensively promoted by Ciba Pharmaceutical Products, Inc. In view of the firm's active campaign of advertising propaganda, the Secretary of the Council asked the firm if it cared to present its product for the Council's consideration. This the firm did in the usual manner, submitting with its presentation a number of advertising circulars.

The Council omitted from New and Nonofficial Remedies all creosote and guaiacol compounds because, after a thorough-going and painstaking inquiry, it was found that evidence is lacking to show that this group of compounds is a necessary part of the modern therapeutic armamentarium (*THE JOURNAL*, Jan. 15, 1938, p. 209). In its examination of the advertising submitted by Ciba Pharmaceutical Products, Inc., the Council found it replete with therapeutic claims which, in view of the Council's investigation referred to, must be held to be unwarranted. For example, the use of Resyl has been proposed in a large number of conditions such as diseases of the respiratory organs, cough, acute and chronic bronchitis, tracheitis, pharyngitis, laryngitis, whooping cough, influenza, measles, tuberculosis and other febrile conditions associated with catarrhal disorders. The product has been claimed to reduce bronchial secretion and facilitate expectoration; however, no attention is called to the fact that it is often necessary to increase secretion in order to facilitate expectoration. No acceptable evidence is offered to support the claim that Resyl-Ciba possesses "all the therapeutic properties of creosote and guaiacol without their disadvantages."

In view of its previous action, and of the nature of the advertising propaganda for Resyl-Ciba, the Council declared the product unacceptable for inclusion in New and Nonofficial Remedies because of unwarranted therapeutic claims.

When the report was transmitted to Ciba Pharmaceutical Products, Inc., the firm replied with various suggestions for revision and with the statement that the advertising was prepared prior to the Council's publication of its revaluation of creosote guaiacol preparations. The firm added that revision of the claims will be made in the next edition of the advertising. The fact remains, however, that the present evidence available serves to show that creosote and guaiacol have no place in the modern materia medica.

Recently E. J. Fellows (*Am. J. M. Sc.* 197:683 [May] 1939) has confirmed the Council's opinion of the lack of pharmacologic rationale for the use of calcium creosote in pulmonary disorders by a controlled investigation of the phenol content and volume of the sputum in a total of fifty-six cases of pulmonary tuberculosis. Tuberculous patients of similar degrees of lung change were selected because such cases provide reliable controls in which more constant daily sputum output is produced than in most bronchial diseases. In spite of adequate absorption as revealed by measurement of the volatile phenols in the urine of patients receiving the highest oral doses of the drug, no significant change in either the sputum phenols or sputum volumes was observed in any of the cases during the period of calcium creosote administration. This study not only contradicts claims that creosote compounds increase expectoration but also invalidates the alleged thesis that any appreciable phenol concentration in the lungs is produced.

Council on Foods

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING
REPORT.
FRANKLIN C. BING, Secretary.

ANNUAL MEETING OF THE COUNCIL ON FOODS, 1940

The annual meeting of the Council on Foods was held at the Association headquarters on March 7 and was attended by the following members:

Dr. Franklin C. Bing	Dr. Lydia J. Roberts
Dr. George R. Cowgill	Dr. Mary Swartz Rose
Dr. Morris Fishbein	Dr. Tom D. Spies
Dr. Philip C. Jeans	Dr. Russell M. Wilder
Mr. Culver S. Ladd	Dr. Arild E. Hansen (proxy for
Dr. Howard B. Lewis	Dr. Irvine McQuarrie)
Dr. James S. McLester	

Several invited guests were also present, including the following members of the Council on Pharmacy and Chemistry:

Dr. H. N. Cole	Dr. E. M. Nelson
Dr. P. N. Leech	Dr. W. W. Palmer

Dr. Fishbein requested that he be relieved of the chairmanship of the Council in order to permit him to devote more time to other activities. Drs. McLester and Lewis were elected Chairman and Vice Chairman of the Council respectively.

Among the topics which were given consideration at the meeting, the following items may be of interest to physicians, manufacturers and others.

Scope of the Council's Activities.—When the Council was first organized in 1929 there was need for a body of experts to express authoritative group opinion about health claims made in the advertising of food products. The Council devised a seal by which manufacturers could make known that they had accepted the Council's requirements for restriction of advertising claims to those which were considered established. It also has been a requirement of the Council that the nature and amount of each ingredient of processed foods be made known and that there be on labels for such foods a complete declaration of ingredients in the order of their decreasing proportion.

The new Food, Drug and Cosmetic Act includes provisions for the more precise labeling of processed foods. Definitions and standards of various classes of foods are being developed. No longer are the provisions of the Council regarding declaration of ingredients of compounded foods so necessary, now that governmental agencies are empowered to deal more adequately with this problem. Further, the Federal Trade Commission has had broad powers conferred on it by reason of the Wheeler-Lea Amendment. This agency now has greater authority to police objectionable claims in advertising. There no longer should exist a need for detailed examination by the Council of much advertising material, although the demand for the Council to provide an authoritative opinion on questions pertaining to foods and health still remains. For these reasons it would seem proper for the Council to consider a revision of its policies to permit the relinquishment of certain functions and the expansion of others.

The Committee on Scope of the Council was charged with the duty of developing a plan whereby the number of food products considered for acceptance might be considerably reduced. Attention should continue to be paid to individual products intended for infant feeding, special foods for feeding the sick, and foods which have been manipulated in such a way as to enhance their nutritional properties, by the addition of preparations of vitamins, minerals or other dietary essentials. It would be well to devote more attention to nutritional claims and interpretations of laboratory and clinical reports on the nutritive properties of foods and diets.

Action was deferred on these questions until after a thorough study could be made of the manner by which the Council might utilize its resources to the fullest possible extent.

Publications.—The book *Accepted Foods and Their Nutritional Significance* has been well received. The book was intended to provide in readily accessible form authoritative infor-

mation about commercial foods, and it is gratifying to note that this purpose seems to have been achieved. Plans were discussed for revision of the book and improvements in the material which it contains, with a view of keeping the volume up to date and having it represent the opinion of the Council on matters of nutritional importance.

The first printing of the Symposium on The Vitamins, published under the joint sponsorship of the Council on Foods and the Council on Pharmacy and Chemistry, has been entirely disposed of. It was voted to authorize the printing of an additional number of copies to meet the anticipated demand for one year, after which the question of the preparation of a new series of articles would be given consideration.

Fortification of Foods with Minerals and Vitamins.—There has been published in the 1939 report of the Council a statement of general policy adopted by the Council with regard to the fortification or restoration of foods with vitamins, minerals and other dietary essentials. As far as general purpose foods are concerned, it was decided that, with few exceptions, fortification of these products could well be restricted to the restorative addition of important nutritional essentials for which a greater intake is considered to be in the interest of public health. In this way processed foods would be brought up to the original high nutritive level of unprocessed foods. A number of specific problems have been presented for the Council's consideration in connection with this rational process of improving the nutritive quality of foods. Breakfast cereal products are usually divided into two classes, the ready-to-eat variety and those which are eaten after cooking. The cereal product having the highest vitamin B₁ content appears to be oatmeal, which may provide as much as 300 international units of vitamin B₁ to each hundred grams of dry material. Whole wheat contains on the average about 165 international units of vitamin B₁ per hundred grams. Most breakfast cereal foods contain considerably less vitamin B₁ than either whole wheat or oatmeal. It was decided that the addition to breakfast cereals of vitamin B₁, in the form of thiamine hydrochloride, up to the level of oatmeal would be in agreement with the Council's previously declared policy. This permits the restorative addition of vitamin B₁ to these products so that they may contain up to 300 units of vitamin B₁ per hundred grams, or 80 units per hundred calories.

While whole grain cereal products are usually considered to be of nutritional value because of the vitamin B₁ (and iron) which they contain, they also provide calories, protein and certain other members of the vitamin B complex. It was decided that no objection would be taken to the restorative addition of substances rich in riboflavin to processed cereal foods. Claims must be restricted to statements of fact, however, such as "this product has been enriched with riboflavin to the value of whole wheat," or the like, because the principal dietary sources of riboflavin are milk and meats, and not cereals, even of the whole grain variety.

The foregoing decisions refer to general purpose foods, which means foods which are ordinarily considered to be useful for any member of a family. Another type of product, the so-called special purpose food, is designed and represented for special dietary use. Items in this class are foods specially treated to make them of value in the diets of infants or invalids, or foods which are designed to provide a convenient, rich source of one or more dietary essentials. The Council requires that the intended dietary use of such special products be mentioned on the label and that the contribution which the product makes to the diet likewise be declared. With respect to the permissible vitamin (or mineral) content of such products, the Council decided that each product would need consideration on its own merits and no limit would be placed on the extent of fortification up to what is considered to be the normal nutritional requirement for a healthy person.

Dietary Advice.—A great deal of advertising for food products partakes of the nature of dietary advice to the general public. There are pamphlets, for example, on how to select foods in order to be provided with what experts in nutrition consider to be the essential components of an adequate diet. Motion pictures likewise have been prepared which purport to convey authoritative advice for the public. Much of the commercial material that has been brought to the attention of the

Council is not as educational as it might well be. This is particularly true of material which has been prepared with the seeming intent of increasing the consumption of some particular food. For example, the increased use of bread and cake and other bakery products prepared from refined cereals and high in carbohydrate content has been urged. While these products are wholesome foods, the inclusion of large quantities of refined cereal products in the dietary requires extraordinarily careful planning of the other components of the diet in order that the essentials for adequate nutrition may be attained. The Council deplores the lack of sound information in much general advertising material which seemingly reaches a vast audience among the general public. It is gratifying to note some exceptions, in addition to material on which the Council's seal is permitted to be displayed. Two pamphlets in particular which appear to be quite commendable are "What to Eat and Why" and "Waist-lines" published by the John Hancock Life Insurance Company.

There has been a tendency for manufacturers and distributors of foods to publish pamphlets embodying special dietary suggestions, particularly diet specifications for reducing purposes. These diets are prepared primarily to show how a particular food product may be included in a restricted ration for reducing weight. While small amounts of many foods, even those of high caloric value per unit weight such as fats, can be included in low-calory rations, it is usually difficult to formulate adequate diets which include significant amounts of foods that supply calories and little else. Of course, small amounts of fat have a flavor as well as a satiety value. They increase the palatability of vegetables. Even a slice of white bread may have some advantages in making a reducing diet more acceptable to the person using it. There is no objection to the preparation of simple directions for the preparation of special diets, but the work should be done by properly qualified persons and the diets suggested should be in accord with what authorities consider desirable. Prolonged use of inadequate diets of low calory value may result in great harm. It is usually necessary to select a caloric intake to fit the needs of the individual patient and to recommend supplements of vitamin-rich preparations or minerals or both in the amounts needed by the individual patient, in order to insure a diet satisfactory in regard to these nutritional essentials. Any person going on a prolonged reducing regimen should be under the care of a qualified physician. Firms which wish to write brochures on the principles of reducing would do well to emphasize these important facts.

The Council is opposed to slipshod methods of offering dietetic advice. The Council is opposed to advertising which overemphasizes the nutritional value of individual foods.

Vitamin D and Growth.—Consideration was given to recent evidence purporting to show that infants fed on milk containing 135 U. S. P. units of vitamin D to the quart, and no other dietary source of vitamin D, exhibit excellent growth. The referee analyzed the data provided in these published reports and called attention to the fact that the growth could be called excellent only if relatively poor standards of achievement were used for comparison. It is well known that vitamin D is a factor in growth. Evidence shows that milk which provides 400 U. S. P. units of vitamin D to the quart permits growth at an optimal rate, whereas milk containing 135 U. S. P. units to the quart does not. The referee emphasized the importance of continuing growth studies on babies over a considerable period of time. It is not so much the growth during the first six months of life as the growth from six months to one year that tells the story. The Council concurred in the referee's views, and the claim that 135 U. S. P. units of vitamin D to the quart yields a milk which produces excellent or optimal growth was considered not established.

Junior Foods.—During the last decade it has become customary to introduce finely chopped or strained foods into the diet of the infant at very early ages. The Council continually has emphasized that it is the function of a physician to decide at what particular age an individual baby is best given supplementary foods and in what quantities. Perhaps the most important value of feeding supplementary foods, such as strained fruits and vegetables, to young infants is the psychologic value of having the baby become accustomed to a variety of foods at an early age. If rightly done, this renders the problem of transferring the baby to the adult type of food much simpler. It is,

after all, a fundamental principle of pediatric feeding to provide the young infant with foods he individually needs with the aim of preparing him for his place in the life of the family.

Strained foods are useful for a limited period, but their long continued use may defeat the main purpose of introducing them into the dietary of the infant. Chopped foods, or so-called junior foods, represent a transition food, likewise of value for a limited time. The Council has opposed any representations that chopped foods should be continued in the diet of a child beyond the age for which they are of particular value. Ordinarily this may be at about 1½ years, with variations depending on the individual child.

The term "junior food," which has been introduced for certain commercial preparations, is considered relatively unobjectionable, provided the claims are properly restricted and an appropriate explanatory statement accompanies the term on labels to indicate the age group for which the products are suited. Vignettes on labels for chopped foods or junior foods are not satisfactory, in the opinion of the Council, if they show children who are obviously older than 1½ years, because they are misleading. This can be corrected by stating prominently, in close proximity to the illustration of the older child, that the product in the can is intended for feeding infants in the range of about 8 to 18 months, depending on the physician's instructions.

ACCEPTED FOODS

THE FOLLOWING ADDITIONAL FOODS HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO ACCEPTED FOODS.

FRANKLIN C. BING, Secretary.

FATS AND OILS AND THEIR PRODUCTS (See Accepted Foods, 1939, p. 30).

The Cudahy Packing Company, Chicago.

PALM BRAND OLEOMARGARINE, containing coconut and cottonseed oils, cultured skimmed milk, salt, sodium monostearosulfacetate as emulsifying agent and sodium benzoate.

Analysis (submitted by manufacturer).—Moisture 15.0%, total solids 85.0%, ash 0.3%, sodium chloride (NaCl) 2.6%, fat (ether extract) 81.4%, protein (N × 6.25) 0.4%, carbohydrates (by difference) 0.5%.

Calories.—7.36 per gram; 209 per ounce.

FRUIT JUICES INCLUDING TOMATO JUICE (See Accepted Foods, 1939, p. 48).

Rio Grande Valley Citrus Exchange, Weslaco, Texas.

TEXSUN BRAND GRAPEFRUIT JUICE, SWEETENED.

Analysis (submitted by manufacturer).—Moisture 86.7%, total solids 13.3%, ash 0.3%, fat (ether extract) 0.03%, protein (N × 6.25) 0.5%, reducing sugar 6.9%, sucrose 3.3%, crude fiber 0.01%, carbohydrates other than crude fiber (by difference) 12.5%.

Chemical titration (1938) showed an average of 0.38 mg. ascorbic acid per cubic centimeter of juice, or 760 international units per hundred cubic centimeters of juice.

Calories.—0.52 per gram; 15 per ounce.

TEXSUN BRAND GRAPEFRUIT AND ORANGE JUICE, SWEETENED, a mixture of grapefruit juice (75 per cent) and orange juice (25 per cent).

Analysis (submitted by manufacturer).—Moisture 86.9%, total solids 13.1%, ash 0.3%, fat (ether extract) 0.03%, protein (N × 6.25) 0.6%, crude fiber 0.01%, invert sugar 6.5%, sucrose 4.2%, carbohydrates other than crude fiber (by difference) 12.2%.

Chemical titration (1938) showed an average of 0.40 mg. of ascorbic acid per cubic centimeter of juice, or 800 international units per hundred cubic centimeters of juice.

Calories.—0.51 per gram; 14 per ounce.

PREPARATIONS USED IN THE FEEDING OF INFANTS (See Accepted Foods, 1939, p. 156).

Libby, McNeill & Libby, Chicago.

LIBBY'S BRAND HOMOGENIZED BABY FOODS FORMULATED COMBINATION No. 10, containing tomato juice, carrots and peas.

Analysis (submitted by manufacturer).—Moisture 90.5%, total solids 9.5%, ash 1.1%, sodium chloride 0.2%, fat (ether extract) 0.1%, protein (N × 6.25) 2.2%, crude fiber 1.0%, carbohydrates other than crude fiber (by difference) 5.1%, calcium (Ca) 0.020%, phosphorus (P) 0.047%, iron (Fe) 0.0019%, copper (Cu) 0.00019%.

Report of titration test (1939) indicates that this product contains 0.026 mg. of ascorbic acid per gram, 0.73 per ounce. Protocols of biologic assay (1939) indicate that this product contains approximately 22.5 U. S. P. units of vitamin A per gram, 639 per ounce; and 0.33 Sherman-Bourquin unit of vitamin G (riboflavin) per gram, 9.4 units per ounce. Rat growth tests have demonstrated the presence of small amounts of vitamin B₁ (thiamin).

Calories.—0.30 per gram; 8.2 per ounce.

THE JOURNAL OF THE
AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JULY 20, 1940

THE PLATFORM OF THE AMERICAN
MEDICAL ASSOCIATION

- The American Medical Association advocates:
1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
 2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
 3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
 4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
 5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
 6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
 7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
 8. Expansion of public health and medical services consistent with the American system of democracy.

NEW OPPORTUNITIES IN HEALTH
BROADCASTING

The Federal Communications Commission has issued a ruling on so-called static-less frequency modulation broadcasting, which is designated by the Federal Security Administrator, Paul V. McNutt, as a development which may "provide the greatest stimulus to education our nation has yet experienced." According to a newspaper release¹ dated May 27, by the Federal Security Agency, the ruling of the Federal Communications Commission gives educational agencies the right to exclusive use of radio bands of ultra-high frequency which were opened up by the commission for the first time in 1938 to commercial broadcasting. More than 300 educational institutions, supported by the National

Committee on Education by Radio, favored the proposal that these high frequency bands be assigned exclusively for educational broadcasts. The United States Commissioner of Education, John W. Studebaker, representing state departments of education and 300 educational organizations at the hearing, estimated that the decision would permit as many as 3,000 local broadcasting stations to be erected.

Stations which use radio bands of ultra-high frequency are said to be moderate in cost compared to conventional broadcasting stations. Educational institutions should be in a good position to provide adequate staffs for such stations by slight increases in their normal radio teaching staffs. It is also anticipated that the number of radio production groups and so-called radio workshops in colleges and universities is expected to increase rapidly as a result of this FCC decision. More than 360 colleges and universities now offer specialized courses in radio. New York and Cleveland are already broadcasting programs over this wave band, and the University of Kentucky has recently received authority for the erection of a station to render radio service to out of the way mountain schools.

This development should be of special interest to the medical profession. The American Medical Association and the National Broadcasting Company in the 1937-1938 and 1938-1939 fall and winter seasons broadcast a special series of radio health programs for use in secondary schools over a nationwide network of stations. A selected broadcast from these series received a first award in its class from the Ninth Institute for Education by Radio. Difficulties were encountered, however, owing to time differences between New York and San Francisco and owing to the differences in the length and spacing of classes in various schools. Many schools which desired to use the network programs were unable to do so because their health classes convened at different times or partially overlapped the broadcasting period or occurred on different days. Radio as a medium for coordination with education seems primarily a local problem not to be solved by network broadcasts, except as network broadcasts can be made supplementary to basic local programs. With the development of new stations, noncommercial in character and devoted to education, it is inevitable that attention will be paid to health education. Local medical societies will find a splendid opportunity for cooperation with frequency modulation broadcasting stations now in existence or to be developed. Already the Vermillion County Medical Society in cooperation with radio station WDAN of Danville, Ill., has been broadcasting health talks in cooperation with city and county schools. The opportunities for bringing into the classroom the authoritative voices of community physicians in health talks or round tables and the use of health dramas with participation by student drama classes will be greater than ever before.

1. Federal Security Agency, U. S. Office of Education, Washington, D. C., May 27, 1940, "FCC Ruling on 'Static-Less' F-M Broadcasting Hailed as Boon to Education and Democracy."

STATISTICS ON POLIOMYELITIS

Dauer,¹ of the United States Public Health Service, provides data on the prevalence of poliomyelitis in the United States in 1939 and also summarizes some of the more important results of experimental investigations on poliomyelitis which were reported in the same year. In contrast to the unusually low incidence of poliomyelitis in the United States in 1938, during which time 1,705 cases and 487 deaths were reported, there was a considerable increase in the number of cases in 1939; in the latter year the number of cases was 7,331, a rate of 5.6 per hundred thousand of population. The case rate was highest in New Mexico, where it was 26.1, but in South Carolina, Arizona and Minnesota the rate was over 20. In three other states, Michigan, Utah and California, the case rates were between 15 and 20. In general, during 1939 the distribution of the disease was characterized by a number of localized outbreaks in different areas of the country in addition to a fairly widespread occurrence in the Mountain states. There was considerable variation in the time when outbreaks occurred in different parts of the country; in Charleston the peak of the epidemic occurred in the middle of May, in Detroit in the week which ended on August 26, and in Los Angeles in the week which ended on September 2, while in other areas of high incidence the peaks of outbreaks were reported in September and October. There was similarly a marked variation in the age distribution of individuals afflicted with poliomyelitis in various localities where epidemics occurred. In Charleston County, S. C., for instance, 68 per cent of the patients were under 5 years of age, while in Genesee County, N. Y., only 14 per cent were under 5 years. In Detroit and Buffalo approximately 30 per cent were under 5 years of age. In older groups, age variations were likewise encountered. As an illustration of this, one may again cite Charleston County, where 22 per cent of the patients were from 5 to 9 years of age, 5 per cent were in the 10 to 14 year old group, and 4 per cent were 15 years of age or over, and Genesee County, where 25, 29 and 30 per cent of the patients were in the corresponding age groups.

With regard to the results of experimental work on poliomyelitis which was reported in 1939, Dauer emphasizes the importance of the work of Armstrong.² This investigator, who was able to infect the eastern cotton rat by intracerebral inoculation with a strain of poliomyelitis virus, has not only been able to maintain the virus through numerous passages in the cotton rat but has also been able to infect mice with the same strain. This discovery promises to make possible laboratory studies on poliomyelitis on a larger scale. These observations, along with further studies on the occurrence of the virus of poliomyelitis in human feces³ and the

isolation of the virus from urban sewage,⁴ as well as other work supported by the National Foundation for Infantile Paralysis, give ample evidence of progress in the experimental study of poliomyelitis.

ABORTIFACIENT PASTES

In spite of repeated warnings against the use of abortifacient pastes, physicians continue to write to *THE JOURNAL* requesting information about such substances. These inquirers have concerned themselves mainly with two products—Leunbach's Paste and Interferin. The Bureau of Investigation of the American Medical Association¹ disclosed that Leunbach's Paste is prepared from a number of substances alleged to include potassium hydroxide, sodium hydroxide, iodine and potassium iodide in an olive oil and cacao butter base. Interferin is claimed to be a paste containing iodine. Such pastes have achieved some degree of popularity in Europe, principally in Germany. Numerous reports have indicated, however, that insertion into the uterus of such pastes has resulted frequently in infections and fatalities. Furthermore, laboratory animals treated with such pastes frequently become poisoned and, in a significant percentage, die.

A recent editorial² again emphasized the danger involved in the use of abortifacient pastes. Nevertheless, numerous inquiries indicate that active promotion of these preparations continues. In recent advertising material it was stated that Interferin, marketed by Keefer Laboratories of Chicago, was effective in 5,000 cases without fatalities. References to scientific publications in medical journals were not cited.

Leunbach's Paste, marketed by Merz & Company, Inc., Newark, N. J., is also advertised without accompanying authentic evidence as to its safety for therapeutic purposes. Leunbach's Paste is recommended as well for the treatment of delayed menses, primary amenorrhea, dysmenorrhea, endometritis and endocervicitis. Merz & Company, Inc., claims that there is little danger of infection. Nevertheless, the firm states, "with reasonable care neither an air nor a fat embolism will follow the injection of Leunbach's Paste." Reports in the literature have indicated that deaths following the use of similar pastes resulted from air embolism, fat embolism and infection. In a news item in this issue (p. 227) the use of this paste by a Minnesota abortionist is described.

The ethical physician will of course refrain from using such preparations. Other persons who have little interest in the welfare of the patient may risk the use of abortifacient pastes simply because the preparation is easy to secure and easy to administer. Reliable physicians will resist the vicious promotion of such preparations.

1. Dauer, C. C.: Pub. Health Rep. 55:955 (May 31) 1940.

2. Armstrong, Charles: Pub. Health Rep. 54:1719 (Sept. 22), 2302 (Dec. 29) 1939.

3. Kramer, S. D.; Gilliam, A. G., and Molner, J. G.: Pub. Health Rep. 54:1914 (Oct. 27) 1939.

4. Paul, J. R.; Trask, J. D., and Culotta, C. S.: Science 90:258 (Sept. 15) 1939. Poliomyelitis Virus in Sewage, Current Comment, J. A. M. A. 114:142 (Jan. 13) 1940.

1. Abortifacient Pastes, J. A. M. A. 98:2155 (June 11) 1932.

2. Abortifacient and Leunbach's Paste, editorial, J. A. M. A. 111:533 (Aug. 6) 1938.

Current Comment

PULMONARY EMBOLISM AND THE WEATHER

Many conditioning factors play a part in the formation of thrombosis and embolism.¹ Recently de Takats and his co-workers² have attempted to correlate the time of occurrence of pulmonary embolism in 100 cases with existent weather conditions. This study involved the preparation of meteorographs for the years 1929-1938. The lengthy time element and small number of cases necessitated the employment of the chi square test in order to justify an opinion that the series of temperature deviations based on the date of embolism was formed in a fashion which was not random. Nevertheless—and perhaps surprisingly—certain correlations between the weather and embolism could be demonstrated: it was found that during the spring and fall periods (which showed the most extensive barometric and thermal fluctuations) more emboli occurred, and the summer months were comparatively exempt. The statistical evidence showed that considerable deviations from the mean temperature also seemed to influence the mobilization of blood clots. The authors continue to emphasize, however, that other predisposing and precipitating factors are known to operate in cases of embolism, and the weather is only one of those which lends itself to registration. The tentative conclusion is offered that the maintenance of a steady external environment may be of benefit to the patient threatened with embolism.

METASTASES AND THE VERTEBRAL VEINS

The behavior of many metastatic tumors and abscesses does not fit readily into accepted explanations for the spread of tumors. The absence of involvement of the lungs in some cases especially has been a constant stumbling block to most theories. Now an anatomic explanation is advanced. Batson,¹ in a series of ingenious and careful injections in animals and cadavers, has demonstrated a large group of veins about the vertebral column which he believes form a recognized system. This system, he suggests, can be added to the others: the pulmonary, the caval and the portal. With its connections this venous system allows the direct spread of tumors and abscesses of the thoraco-abdominal wall anywhere along the system without involving the portal, pulmonary or caval systems. Almost every medical journal provides reports of cases, he points out, which are understandable by the mechanism elucidated by this new system of veins but which are otherwise inexplicable. The vertebral vein complex with its cranial and body-wall connections acts as a separate vein system and may serve as a venous by-pass for the other systems. He suggests the simple term "vertebral

veins" for this system. A large number of unexplained clinical phenomena are now clarified. Although the therapeutic applications cannot be anticipated, this work explains the previously obscure mechanism of certain processes.

UNITED STATES V. AMERICAN MEDICAL ASSOCIATION ET AL.

Recently a widely circulated publication has asserted that the Supreme Court of the United States has definitely decided that the practice of medicine is a trade within the meaning of the Sherman Anti-Trust Law of the United States. Such a statement is not correct. The facts are as follows: On July 26, 1939, the District Court of the United States for the District of Columbia sustained the demurrer of the defendants to the indictment in this case and dismissed the charge against the defendants. The government appealed this ruling to the United States Court of Appeals for the District of Columbia. On March 4, 1940, the Court of Appeals filed its opinion reversing the decision of the District Court and remanded the case to the District Court for a trial on the merits of the indictment. Thereupon the defendants petitioned the Supreme Court of the United States to grant a writ of certiorari to review the decision of the Court of Appeals. The United States filed its brief and argument in opposition to the petition of the defendants for a writ of certiorari and therein asked the Supreme Court of the United States not to review the decision of the Court of Appeals at this time because the government argued that the judgment of the Court of Appeals was not final and the Supreme Court ought not review this case until after a trial was had and all the facts appeared in the record. In its brief the government conceded that the question whether the practice of medicine was a trade was a novel one of sufficient importance for the Supreme Court of the United States to settle but urged that this question be not settled by the Supreme Court of the United States until after a trial of the case, when all the facts would fully appear of record. Apparently the Supreme Court of the United States accepted the argument and suggestion of the government and declined to review the decision of the Court of Appeals at this time. The fact that the Supreme Court of the United States declined to review the decision of the Court of Appeals at this time does not mean, as all lawyers know, that the Supreme Court of the United States approved the opinion of the Court of Appeals but means only that for the present the Supreme Court of the United States is satisfied with the action of the Court of Appeals in sending the case back to the District Court for a trial on the merits. If the result of such a trial should be adverse to the defendants, the question whether the practice of medicine is a trade within the meaning of the language used in the Sherman Anti-Trust Law would still be an open question for the Supreme Court of the United States to decide. The Supreme Court of the United States has not yet decided that the practice of medicine in the District of Columbia is a trade within the meaning of the language of the Sherman Anti-Trust Law.

1. de Takats, Geza, and Jesser, J. H.: Pulmonary Embolism: Suggestions for Its Diagnosis, Prevention and Management, *J. A. M. A.* 114: 1415 (April 13) 1940.

2. de Takats, Geza; Mayne, Alvin, and Petersen, W. F.: The Meteorologic Factor in Pulmonary Embolism, *Surgery* 7: 819 (June) 1940.

1. Batson, Oscar V.: The Function of the Vertebral Veins and Their Role in the Spread of Metastases, *Ann. Surg.* 112: 135 (July) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

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Association

* Deceased.

CHECK AND RECHECK YOUR SCHEDULES

Many thousands of the schedules returned by physicians indicate that physicians have, in many instances, omitted important data or have failed to follow instructions in answering questions.

An example of a frequent omission is the failure to place a cross in the square indicating sex—names are not always certain indexes of sex. The date of birth is frequently omitted. If English is the only language spoken, no mark of any kind should be placed in the language squares; zeros in the squares are only confusing and must be crossed out before the information can be transferred to punch cards. On some schedules the year of graduation from medical school is omitted or, when the year of graduation is given, it does not always agree with the record in the American Medical Directory. A physician cannot be classified both in general practice and in a specialty—put a cross in the square opposite one or the other.

There has been some confusion regarding the designation of the proper specialty. Some physicians have indicated 1 (a) Surgery, under Industrial Practice, when they should have placed a cross opposite either 60.1, Surgery, or 60.6, Orthopedic Surgery. If a physician's practice is Obstetrics and Gynecology he should mark 60.5 but not 60.3, Obstetrics, and 60.4, Gynecology.

The indication of previous military experience has been omitted in many instances. Likewise a number of physicians have recorded no information under the heading "Present Commission Held." Perhaps these physicians have had no previous military experience and do not now hold a commission. It would be helpful if physicians who have had no military experience or do not hold a commission would write above the headings 65. "Previous Military Experience" and 68. "Present Commission Held" the word "none."

In many instances in which some previous military experience has been indicated or a commission in some branch of service has been checked the physicians have failed to state the rank. Please indicate rank accurately. If a commission is held in the Navy, it is important that the grade of Lieutenant be stated thus: Lieutenant, Lieutenant Junior Grade (Asst. Surg.), Lieutenant Junior Grade (Acting Asst. Surg.).

Many physicians have omitted a check for question 74. "In the event of war, will you volunteer for military service?" Yes ☐ No ☐. An answer to this question

merely indicates a voluntary disposition on the physician's part to offer his services to the military establishment. If undecided at this time, the physician should indicate by writing the word "undecided" in the margin and leaving the squares blank.

PHYSICIANS NEEDED FOR ARMY SERVICE

The physician, like every other American, has become actively interested in our national security and stands ready to contribute his services as required for military preparedness.

The immediate problem in this connection is one that concerns the War Department, and primarily the young physician. The War Department must procure sufficient additional personnel from the medical profession to augment the medical services of the Regular Army as the various increases are made in the strength of the Regular Army, as authorized by Congress to meet the partial emergency. The young physician is especially concerned because it is usually advantageous, and is often more convenient, for him to serve with the Army.

Present plans of the War Department are designed to make service attractive and instructive for the young physician. If the physician holds a Medical Corps Reserve commission he can be ordered to active duty if he so requests. If he does not hold a commission but is under 35 years of age and is a comparatively recent graduate of an accredited school, he may secure an appointment in the Medical Corps Reserve for the purpose of obtaining extended active duty for a period of one year or longer. Duty is given at general hospitals, station hospitals, and with Tactical Units, and embraces all fields of general and specialized medicine and surgery. Excellent postgraduate training is obtainable in connection with Aviation Medicine. After serving six months of active duty in the continental United States, a Reserve officer may request duty in Hawaii, Panama or other United States territories and possessions. The initial period for duty is for one year and yearly extensions are obtainable thereafter until the international situation becomes more clarified and our domestic military program becomes stabilized.

Many young doctors who have served with the Army on extended active duty have taken the competitive examination for entrance into the Medical Corps of the Regular Army. Extended active duty affords an excellent opportunity for the physician to observe modern military medicine and the facilities that exist for a complete and comprehensive medical practice.

Pay is according to rank and, including subsistence and quarters allowances for an officer with dependents, amounts to an annual sum of \$3,905 for a Captain and \$3,152 for a First Lieutenant; or, without dependents, to an annual sum of \$3,450 for a Captain and \$2,696 for a First Lieutenant. In addition, reimbursement is made for travel to duty station and return.

Further information may be obtained by writing to the Surgeon General, U. S. Army, Washington, D. C.

ORGANIZATION SECTION

MEDICAL ECONOMIC ABSTRACTS

FARM SECURITY SERVICE IN LOUISIANA

Beginning April 1, 1939, eleven of the thirteen doctors in Avoyelles Parish, La., agreed to serve 250 families who joined the medical group of the Farm Security Administration out of 400 families receiving FSA assistance. Contributions varying from \$10 to \$24 per family were put into a fund from which to pay for medical services and drugs for a year. The patients had only to present their medical card to the doctors of their choice belonging to the Parish Medical Society. The fees were nominally \$2.50 for an office visit, \$3.50 for house calls, including medicine in both cases, 25 cents for each mile after 2 miles, \$25 for obstetric cases, \$5 for minor surgery and from \$15 to \$25 for fractures.

The total amount in the fund was \$3,200 divided into twelve instalments of \$266.50 each, which amount was shared among the physicians furnishing service in proportion to the amount of their bills rendered. The total bills for the year were \$5,800, of which the physicians received \$3,200. This amounted to an average collection of 55 per cent, out of which the doctors had to pay for drugs, which amounted to about 35 per cent of the amount collected and left the doctor receiving about 36 per cent of his fees. The average doctor booked \$527 and collected \$291, of which \$100 went to a druggist. It was the unanimous opinion of the doctors represented in the Parish Medical Society that, since they could not make a living collecting 36 per cent of these fees, they did not therefore feel justified in continuing the FSA plan. As a whole the patients did not abuse the service with excessive demands, and the doctors tried to keep unnecessary visits at a minimum and had as few house visits as possible. Since it was believed it would not be possible for this group to contribute any larger amounts, the doctors decided that they preferred to charge and collect from each patient as an individual.

MEDICAL EDUCATION IN GERMANY

In the educational magazine *Die Erziehung*, published in Leipzig (14:344 [May] 1939), there appeared an article by Hans Wenke entitled "Pedagogic Conditions in Germany." That portion of the article which relates to medicine is here translated:

REORGANIZATION OF THE STUDY OF MEDICINE

The university reforms carried out in recent years within the framework of national socialist cultural and educational policy have been most noticeable in those branches of science in which the innovations were responsible for a reorganization of the course of study. Such was the case in all branches in which a precise semestrial division of the matter of instruction was previously laid down. Let us recall the reorganization of the study of law, economics, agricultural economics, forestry and the university training of teachers previously reported in this journal.

The reorganization of the study of medicine and of several allied courses of study was effected quite recently in like manner. It was prompted by various motives. To begin with, an abbreviation of the study of medicine became necessary for sociological reasons and, as a result of the latest development of research and politico-philosophical considerations, new fields of study came into the limelight and were added significantly to the curriculum. These measures could be harmonized only by a thorough reorganization of the complete course. The reform implied the cooperation of two ministerial authorities, as the ministry for the interior regulates the requirements and conduct of medical examinations while the ministry of education is responsible for the course of study.

The decree emphasizes the fact that the abbreviation of the duration of medical training, like the abbreviation of other academic professions, became an imperative necessity for sociological and economic reasons. This is obtained in this instance by requiring four semesters instead of five for admission to the preliminary medical examination in anatomy and physiology. The medical preliminary examination has consisted up to the present of a section of natural sciences (chemistry, physics, zoology, botany) and a section of anatomy and physiology (anatomy, general physiology, physiologic chemistry). The requirement of admission to the first section used to be two semesters and, to the second section, three additional semesters. It is the aim at present to combine these two sections. As the clinical training for six semesters is retained, the complete medical course lasts ten semesters.

A further measure will consist in abbreviating the duration of the medical final examination. Heretofore this has been spread over two semesters on the average, with a maximum time allowance of two years.

The most important and decisive innovation, however, consists of including in the course of study the one year period of practical training. Until now this was done following the final examinations and the physician had to serve one year of successful internship at a university clinic, polidinic or designated hospital before being permitted to practice. From now on this will be done through practical work during the semester and through working as an assistant during vacation. This regulation can be easily fitted into the new order of studies, which was designed more especially to meet the requirements of the practicing physician with consequent emphasis on the parallel completion of theoretical studies and practical training. Besides nursing and medical service in the air defense corps, obligatory service in the rural districts or in industrial establishments have been added to the curriculum. This used to be done voluntarily. It will last six weeks and should be completed in the vacation between the third and fourth semesters. The assistantship of six months will be completed in two parts in the vacation periods between the seventh and eighth and between the ninth and tenth semesters. At the university clinics it is permitted only in surgery, internal medicine, gynecology and pediatrics. The second part of the assistantship should be completed in a different branch.

The reorganization is further characterized by the arrangement of the courses of study. In doing this the development of modern medical research in new fields and the sociological duties of the physician in the Third Reich were taken into consideration. On the initiative of the national physician leader and of the leader of the national association of university instructors, new obligatory lectures have been added to the curriculum such as history of medicine, medicinal herb excursions, work, sport and military physiology (flying included), policies relating to population and others in the preclinical part; radiology, natural therapy, heredity and eugenics, occupational diseases, child welfare, emergency treatment, social insurance and examination, medical jurisprudence, professional ethics and others, in the clinical part.

The reorganization, besides responding to an actual sociological necessity, represents the fulfilment of requirements brought about by the inner changes of the science of medicine and the amplification of practical medical duties. On this question the statements of Ferdinand Sauerbruch published in this journal approximately two years ago are of interest. Sauerbruch pointed out convincingly the theoretical as well as practical aspect of the study of medicine and the requirements resulting therefrom.

Naturally it cannot be overlooked that courses of study merely create the administrative requirements for the successful fulfilment of new tasks; the realization of the higher requirements, however, depends on the personal ability of the students. In

explaining the reorganization, the secretary of education emphasized this circumstance by pointing out that the intensified curriculum should serve as an incentive to make up by industry and concentration for the time saved; he emphasized that the duties and responsibilities of the practicing physician became greater in the national socialist state, voicing thereby the general conviction that the problems of university reform have been lately of a moral rather than of an administrative-technical character.

It will be noted that under the new regulations the length of the medical (and premedical) course is reduced to ten semesters, or five years, as contrasted with the seven or eight year program which prevails in the United States. Notwithstanding this abbreviation of the course, new subjects are to be required, among them "medicinal herb excursions," a strange anachronism. The "assistantship," so called, would appear to correspond much more closely to a clinical clerkship than to an internship, since it is interposed between the seventh and eighth and between the ninth and tenth semesters. Obviously the undergraduate student is not prepared to assume the responsibilities which we associate with the function of an intern.

LEGAL SERVICES FOR LOW INCOME CLASSES

The close parallelism between the problems of the legal and the medical profession is shown by recent discussions in the *American Bar Association Journal*.¹

The Bar Association has a Committee on Legal Service Bureaus, which in its report to the house of delegates of the American Bar Association in Chicago in 1939 said:

For some time it has been felt in many quarters that the organized bar of this country though adequately serving those able to pay substantial fees, and though adequately serving those in need of legal aid without charge, may be derelict in a duty to a vast middle group, which may be referred to as "the low income group." It has been suggested, accordingly, that the lawyers themselves should provide bureaus to furnish such legal aid at nominal charge. Experiments are now being conducted in Phila-

delphia and are about to be undertaken, if not already under way, in Chicago, New York, Minneapolis, San Francisco and other large cities. In general, the proposals are that the work should be confined to a group with incomes up to \$2,000, it being felt that such a group do not deserve free legal aid and, on the other hand, do not want to be pauperized, in a sense, by having to resort to a purely charitable institution. It is felt that on the other hand they cannot pay the fees required and deserved by the larger and better established law firms. It is also suggested that in this way we shall not be taking away from the practice of any lawyer, but be adding to the total amount of legal service available to the public.

The plans in contemplation for operation propose neighborhood law offices equipped to handle matters of a minor nature on a self-sustaining basis. It is felt that younger lawyers and lawyers without sufficient practice otherwise to employ their full time can competently staff those bureaus; and, in view of the quantity of work and the specialized nature, will be able, for small fees, to take care of the requirements of persons in the group referred to, the schedule of fees generally to run from \$2 or \$3 for a conference up to \$10 for matters of greater scope, with or without provisions for handling claims such as personal injury claims, on a contingent basis.

The committee is confronted with the suggestion that organized society may set up bureaus to compete with individual lawyers and that, unless the bar associations act, something of this nature will be forced on the profession. The data available to the committee were so extensive that it did not feel ready to make definite recommendations. No member of the committee had any criticism for the system of free legal aid bureaus, which, as already noted, exist in several large cities. The committee therefore recommended further investigation and invited suggestions and discussions from the members of the association.

It is also significant that examples of similar action are sought for in Europe. Lloyd K. Garrison, dean of the Law School of the University of Wisconsin, reports on a study made in Sweden on the occasion of a visit there.² The Swedish Free Legal Proceedings Act of 1919, in connection with the "Public Institutes for Legal Assistance," which correspond to our legal aid bureaus, provides for an extensive system of free and low cost legal services. The Public Institutes are governmental undertakings, the first of which was founded in Gothenburg in 1872 and which now exist in the principal Swedish cities.

Dean Garrison also describes the Milwaukee Legal Aid Bureau and compares it with the Stockholm institutes, finding that the cost and scope of the work done in Stockholm are much greater although the two cities are of much the same size.

1. Report of the Committee on Legal Service Bureaus, Am. Bar A. J. 26: 125 (Feb.) 1940.

2. Garrison, Lloyd K.: Legal Service for Low Income Groups in Sweden, Am. Bar A. J. 26: 215 (March) 1940.

WOMAN'S AUXILIARY

Alabama

The annual meeting of the auxiliary to the Medical Association of the State of Alabama was held in Birmingham April 16-18. Mrs. J. U. Reaves was president during 1939-1940. There are seven active auxiliaries to county medical societies in Alabama, having a membership totaling 211.

The auxiliary to the Jefferson County Medical Society has met regularly in Bessemer. Doctors' Day was observed in March and a public relations meeting was held. The auxiliary maintains a Loan Closet for the use of indigent persons at the Bessemer Health Center.

Florida

Mr. T. E. Middlebrooks, district supervisor, U. S. Bureau of Narcotics, spoke on "The Narcotic Problem" at a meeting of the auxiliary to the Duval County Medical Society in Jacksonville, March 7.

Georgia

The auxiliary to the Baldwin County Medical Society held its March meeting in Milledgeville. The auxiliary was awarded a first prize in the recent *Hygieia* contest.

Dr. J. C. Patterson, president-elect of the Medical Association of Georgia, discussed "The Need for an Auxiliary" at a meeting of the auxiliary to the Tenth District Medical Society in Augusta, February 14.

The auxiliary to the Fulton County Medical Society held a public meeting recently at the Academy of Medicine in Atlanta. The speakers were Dr. Clarence Laws, "Allergy and Hay Fever"; Dr. Jack Norris, "Milk in Relation to Health," and

Dr. Glenville Giddings, chairman, health education committee of the medical society.

Dr. Harold W. Muecke spoke on child welfare and Dr. Marvin Harris on the treatment of hookworm at a recent meeting of the auxiliary to the Ware County Medical Society in Waycross.

Iowa

The auxiliary to the Polk County Medical Society met in Des Moines March 5. Speakers were Dr. Howard D. Gray, president of the Polk County Medical Society, and Dr. John H. Peck, superintendent of the State Sanatorium at Oakdale. Students from Drake University gave a musical program.

Louisiana

The auxiliary to the Caddo Parish Medical Society met in Shreveport, March 13. Dr. J. H. Musser, New Orleans, discussed "The Problems of State Medicine and How the Doctor Looks at Them."

The auxiliary to the Calcasieu Parish Medical Society entertained the auxiliaries to the Beauregard and Jefferson Davis parish medical societies in Lake Charles recently. Mrs. S. M. Blackshear, president of the auxiliary to the Louisiana State Medical Society, was speaker.

The chief philanthropic work of the auxiliary to the Terrebonne Parish Medical Society during the year was providing eyeglasses for needy school children.

Auxiliaries to the Beauregard and LaFourche parish medical societies have recently been organized.

Grant for Research in Pediatrics.—The committee on the Elizabeth McCormick Child Research Grant of the Institute of Medicine of Chicago announces that it has the sum of \$1,500 to be awarded to qualified investigators in the Chicago area for the aid of research in child welfare. Projects should in a broad sense be in the field of pediatrics, it was said. Applications by letter will be received up to October 15 and the award will be made soon after that date. Address all communications to Dr. John Favill, secretary of the committee, 122 South Michigan Avenue, Chicago.

INDIANA

The Boy Scout Committee.—For the past ten years the boy scout committee of the Indianapolis Medical Society has provided medical attention for the scouts who attend the summer camp at the Scout Reservation, according to the society's bulletin. The average attendance is about 250, making it necessary to employ a resident physician. The fund to pay the physician was started by Dr. John W. Carmack and has been perpetuated by special gifts, popular subscription and "sustaining memberships" of \$10 each, from the membership of the society. The annual sum needed has been from \$150 to \$200. At a meeting, May 21, on a motion sponsored by the boy scout committee, the society voted to designate this fund as "The John W. Carmack Memorial Fund." The money raised each year is to be held by the treasurer of the scout council and be expended as directed by the boy scout committee of the society to defray the medical expenses at the scout camp. In addition to the first-aid care of illness and accidents, the committee acts in an advisory capacity in maintaining the proper sanitation. There has also been a continuous effort to teach the boys the principles of health hygiene. This instruction reaches about 1,200 boys annually. Donations may be made through the secretary of the society or through the chairman of the boy scout committee.

MAINE

Society News.—Clarence C. Little, Sc.D., Bar Harbor, presented a "Review of Cancer Control Programs in Other States with a Discussion of Changes in Our Own State Program" before the Cumberland County Medical Society in Portland, May 23.—A panel discussion on head injuries was conducted before the Portland Medical Club recently by Drs. Erastus E. Holt Jr., Francis W. Hanlon, Harry E. Macdonald Jr. and Charles H. Hunt.—The Kennebec County Medical Association was addressed in Togus, May 16, by Dr. Joe Vincent Meigs, Boston, on "Female Endocrinology."

MINNESOTA

Abortionists Sentenced.—William E. McCoy, St. Paul, aged 35, pleaded guilty, April 1, in Hennepin County to practicing healing without a basic science certificate and paid a fine of \$500. He also pleaded guilty to performing a criminal abortion and received a sentence of four years in the state reformatory at St. Cloud, which was suspended. On May 13, Samuel M. Stern, a licensed osteopath, and Agnes L. Shanks, his office assistant, pleaded guilty in the district court of Ramsey County to an information charging them jointly with the crime of abortion. Both were sentenced to terms not to exceed four years at hard labor. Several deaths have been attributed to Stern's activities as an abortionist, it was stated. In two cases handled by Stern state authorities are reported to have found that Leubach's paste, a product of Merz & Company Chemical Works, Inc., Newark, N. J., was used. In their report, they state that evidence found in the recent case in which Stern and Shanks were apprehended indicates the danger of using this paste. The report further states that it is hoped that state and federal authorities will find a way to deal effectively with the sale of this product in Minnesota.

MISSOURI

Dr. Schorer Resigns as Director of Health.—Dr. Edwin H. Schorer has resigned as director of health of Kansas City, effective May 23, newspapers reported. He held the position five years.

Ricketts Prize Awarded to Pathologist.—Harold R. Reames, Ph.D., now a pathologist at Washington University School of Medicine, St. Louis, has been awarded the annual Howard Taylor Ricketts Prize by the University of Chicago for his research on a local virus infection of the upper respiratory tract. Dr. Reames' research was done at the University of Chicago during his graduate studies. He received the degree of doctor of philosophy from the University of Chicago in 1940.

Casselberry Prize Awarded to Dr. Hansel.—The Casselberry Prize of the American Laryngological Association was awarded to Dr. French K. Hansel, assistant professor of clinical otolaryngology, Washington University School of Medicine, St. Louis, during the annual meeting of the association in May in Rye, N. Y. The prize was given to Dr. Hansel for original cytologic observations of the secretions of the nose and sinuses in allergy. Dr. Hansel graduated at St. Louis University School of Medicine in 1918. The Casselberry award was established by the late Dr. William E. Casselberry, Chicago, when he devised a fund to the American Laryngological Association, the interest to be awarded in sums of \$500 or less for outstanding work in laryngology and rhinology.

MONTANA

Society News.—John X. Newman, B.S., Butte, was elected president of the Montana Public Health Association at the annual meeting in Bozeman in June, and Dr. William F. Cogswell, Helena, secretary.—The Chouteau County Medical Society was recently organized at Fort Benton, with Dr. Denton J. Cooper, Big Sandy, as president.

State Medical Election.—Dr. William E. Long, Anaconda, was named president-elect of the Montana State Medical Association at the annual meeting in Bozeman, June 18, and Dr. James I. Wernham, Billings, was installed as president. Dr. Herbert T. Caraway, Billings, was elected vice president and Dr. Thomas F. Walker, Great Falls, reelected secretary.

NEW HAMPSHIRE

State Medical Election.—Dr. Ezra A. Jones, Manchester, was elected president of the New Hampshire Medical Society at the annual meeting in Manchester in May. Dr. Charles H. Dolloff, Concord, was elected vice president and Dr. Carleton R. Metcalf, Concord, reelected secretary. Fifty year gold medals were presented to Drs. Arthur K. Day, Concord; Frank E. Kittredge, Nashua, and George H. Gray, Hyannis, Mass.

NEW YORK

Society News.—Dr. Charles M. Carpenter, Rochester, was elected president of the New York State Association of Public Health Laboratories at the annual meeting in Rochester in May; Dr. Francis F. Harrison, Cooperstown, vice president, and Mary B. Kirkbride, Albany, was reelected secretary.—Drs. Clayton W. Greene, Buffalo, and David D. Rutstein, Albany, addressed the Ontario County Medical Society at its quarterly meeting in Geneva, July 9, on "The New Aspects of Treatment and Control of Pneumonia," and Dr. John R. Williams and Arthur C. Parker, Rochester, on "The Use of Hobbies in Therapeutics."

New York City

Thirty-Five Years in Health Department.—Dr. Jules Leon Blumenthal, director of the bureau of child hygiene in the New York City Department of Health, will retire September 1. Dr. Blumenthal began his work with the health department in 1905 as a medical inspector and advanced through civil service examinations to various positions, becoming director of the bureau of child hygiene in 1924.

Physicist Receives Janeway Medal.—Edith H. Quimby, A.M., associate physicist of Memorial Hospital for Treatment of Cancer and Allied Diseases, received the Janeway Medal at the annual meeting of the American Radium Society in New York, June 10. The medal has been awarded annually since 1937 to the Janeway Lecturer at the society's annual meeting, and in that year medals were presented to all who had delivered the Janeway Lecture since it was established in 1933 in honor of a pioneer radium therapist, Dr. Henry Harrington Janeway. Mrs. Quimby's lecture was on "The Specification of Dosage in Radium Therapy."

Honorary Degrees.—Dr. Nathan B. Van Etten, President of the American Medical Association, received the honorary degree of doctor of public health from New York University College of Medicine, June 5.—Dr. Alfred E. Cohn of the Rockefeller Institute for Medical Research received the honorary doctorate of science from Columbia University at its June commencement.—Drs. Herbert S. Gasser, director of the Rockefeller Institute for Medical Research, and Eugene L. Opie, professor of pathology, Cornell University Medical College, received the honorary degree of doctor of laws at the annual commencement of Washington University, St. Louis.—Dr. Stuart Leasley Craig received the honorary degree of doctor of science from his alma mater, the Medical College of Virginia, Richmond, at the commencement, June 4.

Memorial to Pioneer in Miami Valley.—A granite monument to Dr. John Hole, the first physician in the Miami Valley, was unveiled in Centerville, Montgomery County, May 31. Speakers at the ceremony were Drs. Benjamin R. McClellan, Xenia, chairman of a committee that raised funds for the memorial; Walter M. Simpson, Dayton, secretary of the committee, and former Gov. Myers Y. Cooper. The monument is on a roadside plat near where Dr. Hole began practice and near the cemetery in which he is buried. According to information furnished by his descendants, Dr. John Hole was born in New Jersey in 1755 and educated in Germany. He served in the Revolutionary War on the staff of Gen. Richard Montgomery, for whom Montgomery County was named at Dr. Hole's suggestion. Dr. Hole left New Jersey for the Middle West in 1786, settling first in Kentucky and then in Cincinnati, where he remained until 1797. In the latter year he settled about 6 miles from Dayton and founded the town of Woodbourne, now practically deserted. Dr. McClellan started the movement and, besides Montgomery, the following counties joined in the contributions for the monument: Greene, Clinton, Butler, Preble, Clark, Miami, Darke, Champaign and Warren. The First Baptist Church of Centerville, successor to the Sugar Creek Baptist Church, of which Dr. Hole was a member, donated an acre of land for the memorial. The committee in charge of raising the funds was as follows: Drs. Edwin M. Huston, Dayton, chairman; Alonzo H. Dunham, Dayton; Benjamin W. Dudley Keever and Charles D. Slagle, Centerville; Dr. Simpson and Dr. McClellan.

OREGON

Society News.—Dr. Ray W. Hausler, Portland, addressed the Multnomah County Medical Society, Portland, May 15, on "Streptococcic Infection in Relation to Pathological and Clinical Findings."—Dr. Robert Yorke Herren, Portland, addressed the Central Willamette Medical Society in Albany recently on "Recognition and Early Treatment of Acute Head Injuries."—A symposium on "Fluid Administration by Parenteral Methods" was presented before the Yamhill County Medical Society, McMinnville, recently by Drs. Albert W. Holman, Louis P. Gambee, Homer P. Rush and Thomas D. Robertson, all of Portland.

University Medical Library Dedicated.—The University of Oregon Medical School, Portland, dedicated a new library and auditorium in Sam Jackson Park, June 7. Dr. John E. Weeks, honorary professor of ophthalmology in the medical school, who contributed the first \$100,000 toward the building, laid the cornerstone and later a plaque honoring Dr. Weeks was unveiled in the main entrance hall of the library. Dr. Richard B. Dillehunt, dean of the medical school, presided and the speakers included Dr. Frederick A. Kiehle, Dr. Weeks, Chancellor Frederick M. Hunter of the state board of higher education and Donald M. Erb, Ph.D., president of the university. In addition to the donation by Dr. Weeks, funds for the library were provided by the Rockefeller Foundation (\$100,000) and the Public Works Administration (\$163,000).

PENNSYLVANIA

District Meeting.—The Eleventh Councilor District of the Medical Society of the State of Pennsylvania held a meeting in Johnstown, June 20. Dr. Eugene P. Pendergrass, Philadelphia, gave an address on "Silicosis" and Dr. Henry T. Price, Pittsburgh, on "Bringing Infant Feeding Up to Date." Addresses on activities of the state society were made by Drs. Francis F. Borzell, Philadelphia, president-elect; Chauncey L. Palmer, Pittsburgh, chairman of the committee on public health legislation; Belford C. Blaine, Pottsville, chairman of the commission on diabetes, and David E. Hemington, Uniontown, member of the committee on industrial health. Fifty-year certificates were presented to Drs. Jason G. Hanks, Everett, William E. Matthews, Johnstown, and William N. Pringle, Johnstown.

Philadelphia

Postgraduate Lectures.—Mercy Hospital presented its seventh annual course of postgraduate lectures under the auspices of its attending staff, May 13, 15 and 17. Four lectures each were presented on diseases of nutrition, diseases of the abdomen and diseases of the chest.

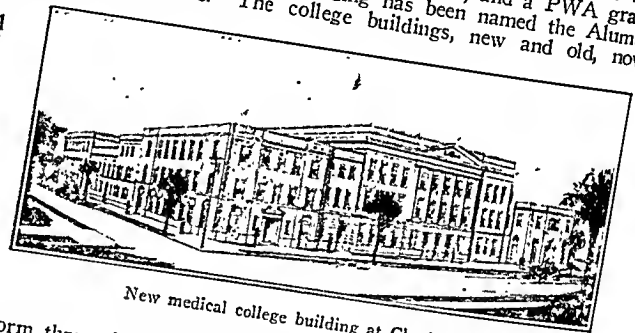
Honorary Degrees.—George H. Meeker, Ph.D., dean and professor of biochemistry, University of Pennsylvania Graduate School of Medicine, received the honorary degree of doctor of science from the university at the commencement, June 12. The same degree was conferred on Dr. Samuel McC. Hamill, for several years head of the state emergency child health committee, and president of the Philadelphia Child Health

Society.—Dr. Henry K. Mohler, dean and Sutherland Professor of therapy, Jefferson Medical College, received an honorary degree from Juniata College, Huntingdon, in June.

University to Have Cyclotron.—Mr. William H. Donner, retired industrialist, has given to the University of Pennsylvania \$200,000 for construction of a cyclotron primarily for research on the treatment of cancer. This will be the third largest now in operation, which is in the laboratory of Ernest O. Lawrence, Ph.D., at the University of California. The second is now under construction at the Carnegie Institution of Washington. The new apparatus will be installed in a special building adjoining the department of radiology, in the rear of a new unit of the University Hospital now in process of construction. The instrument will weigh 250 tons and will generate energy equivalent to that of about 200 pounds of radium. Two technicians will be employed for the treatment of cancer: first, the bombardment of various chemicals, which, thus being rendered radioactive, can be administered to patients, and, second, direct application to the patient of a beam of neutrons. This gift from Mr. Donner, who in 1932 established the International Cancer Research Foundation, brings to \$400,000 his gifts to the bicentennial fund of the university. In 1937 he donated \$200,000 to establish the William Henry Donner Jr. Department of Radiology in memory of his son.

SOUTH CAROLINA

New Medical College Building.—The Medical College of the State of South Carolina, Charleston, recently dedicated a new building which contains facilities for the school of nursing and the school of medicine and for clinical work. Funds for the building were furnished by the alumni association of the medical school, which contributed \$172,000, and a PWA grant of \$141,000. The clinic building has been named the Alumni Memorial Clinic. The college buildings, new and old, now



New medical college building at Charleston.

form three sides of a rectangle which occupies more than two blocks. At the dedication ceremony it was announced that \$125,000 had been given anonymously for an auditorium that will complete the rectangle. The speakers at the dedication were Gov. Burnett R. Maybank; Drs. Robert Wilson, dean of the medical college; Thomas A. Pitts, Columbia, of the board of trustees; Leonidas M. Stokes, Walterboro, assistant professor of anatomy; James R. Desportes, Fort Mill, president of the alumni association; Mr. H. A. Wortham, regional director of PWA, and A. Stanley Llewellyn, of the American Legion. The Legion presented its plaque for distinguished service to Dr. Wilson as part of the ceremony. Preceding the dedication of the building, memorial tablets were unveiled honoring the memory of chairmen of the board of trustees and deans of the college since its founding in 1824.

TENNESSEE

Personal.—Dr. George W. Jackson, Western State Hospital, has been appointed health officer of Bedford County.—Dr. Roscoe Faulkner, Trenton, has been appointed health officer of Williamson County to succeed Dr. Don C. Peterson, Franklin, who has been appointed director of vital statistics in the state health department.—Dr. Benjamin F. Byrd, Nashville, has been appointed medical director of the National Life and Accident Insurance Company, Nashville, to succeed the late Dr. Rufus E. Fort.

Dr. Goodpasture Receives Alvarenga Prize.—The College of Physicians of Philadelphia awarded the Alvarenga Prize, July 14, to Dr. Ernest W. Goodpasture, professor of pathology, Vanderbilt University School of Medicine, Nashville, for his outstanding contributions to the knowledge of viruses. This prize was established by the will of Pedro

Francisco de Costa Alvarenga, Lisbon, Portugal, an associate fellow of the College of Physicians, to be awarded annually by the college on the anniversary of Alvarenga's death, July 14, 1883, to the author of the best memorial on any branch of medicine which may be deemed worthy of the prize.

WEST VIRGINIA

Society News.—Dr. James J. Joelson, Cleveland, addressed the medical societies of Monongalia, Marion and Harrison counties at a meeting in Morgantown, recently on "Tumors of the Adrenal Gland."—Dr. Henry H. Dixon, Portland, Ore., addressed the Kanawha Medical Society, Charleston, in May on management of anxiety states and care of the psychic components of organic disease.—Dr. Warren T. Vaughan, Richmond, Va., addressed the Fayette County Medical Society, Fayetteville, June 25, on practical phases of allergy.

Personal.—Dr. Norman G. Angstadt, Fayetteville, recently health officer of Hancock and Wetzel counties, has been appointed health officer of Fayette County. He succeeds Dr. Leon A. Dickerson, who resigned to join the staff of the state health department.—Dr. Albert M. Price, head of the division of communicable diseases in the state department of health, Charleston, has been appointed health officer of Kanawha County to succeed Dr. Turner E. Cato, who recently became health officer of Dade County, Fla.

Summer Postgraduate Courses.—The West Virginia State Medical Association and the West Virginia State Health Department are presenting courses in obstetrics and pediatrics in ten towns from July 15 to August 23. The speakers who will lecture on the circuit the first two weeks are Drs. Hugh J. Morgan, Nashville, Tenn., and Charles F. Mohr, Baltimore, one week each on "Diagnosis and Treatment of Cardiovascular Syphilis," and John H. Randall, Iowa City, "Obstetric Hemorrhages." The last three weeks Dr. Robert A. Lyon, Cincinnati, will lecture on pediatrics in five towns and Dr. Jay M. Arena, Durham, N. C., in the remaining five. The towns are Montgomery, Beckley, Logan, Welch, Lewisburg, Weirton, Moundsville, Terra Alta, Weston and Keyser.

GENERAL

Award for Study of Diseases of Chest.—The American Association for Thoracic Surgery awarded the first Rose Lampert Graff prize of \$250 to Dr. Paul W. Gebauer, Cleveland, at its meeting in Cleveland in June for a paper on cancer of the lungs. Dr. Gebauer graduated from Western Reserve University School of Medicine, Cleveland, in 1933. The prize was given by the Rose Lampert Graff Foundation of Los Angeles, established in 1939 by Mr. and Mrs. Ellis Levy in memory of Mrs. Levy's mother. Dr. Jacob J. Singer, Los Angeles, is director of the fund. The foundation offers a similar prize through the American Association for Thoracic Surgery for 1941. Any one who wishes to submit a paper should send it to Dr. Richard H. Meade Jr., secretary, 2116 Pine Street, Philadelphia.

Awards in the Physicians' Art Exhibit.—Prizes awarded in the third annual exhibition of the American Physicians' Art Association during the annual session of the American Medical Association in New York, June 10-14, were as follows:

First prize, given by Dr. Max Thorek, Chicago, for the best work of art in the exhibit, to Vela E. Brichta, D.D.S., New York, for a plaster group, "Mother and Child."

Hoffman-La Roche Prize for the best oil, to Dr. Robert H. Kennicott, Los Angeles, for "Figure in Repose."

Prize given by Dr. Charles Homer Wheelon, Seattle, for oil showing highest creative ability, to Dr. William W. Wright, West Hartford, Conn., for "Polish New England."

Prize offered by John Wyeth and Brother for best water color, to Dr. John Groopman, New York, for "Fulton Dock."

Prize offered by G. D. Searle & Company, for best piece of sculpture, to Dr. Abraham L. Wolbarst, New York, for "The Nazarene."

Prize offered by the *New York Physician* for best work by a physician in the metropolitan area, to Dr. Alfred Braun, New York, for an oil, "Girl with Muff."

Prize offered by Winthrop Chemical Company for photographic work, to Dr. James O. Fitzgerald Jr., Richmond, Va., for "Birches by the Brook."

Prize for best etching, to Dr. Josef Warkany, Cincinnati, for "November."

Appeal for Medical Supplies for England.—An urgent appeal for surgical instruments and hospital supplies to be sent to England has been issued by "Bundles for Britain," a volunteer organization licensed by the State Department to ship through the Allied Relief Fund directly to the British Red Cross. England is setting up large numbers of "subhospitals" and hospital bases throughout the country. Instruments and equipment, even if somewhat out of date, are desired. Urgent appeals have been made for bronchoscopes, esophagoscopes, sigmoidoscopes, cystoscopes, bladder retractors, intesti-

nal clamps, forceps of various kinds and sizes, syringes, plaster shears, mouth gags and rubber sheeting. A detailed list will be sent to any one who wishes to help. The address of Bundles for Britain is 484 Park Avenue, New York.

Fellowships in the Medical Sciences.—Thirteen fellowships in the medical sciences, including five renewals, for study in the United States during the year 1940-1941, were awarded at the recent meeting of the Medical Fellowship Board of the National Research Council, Washington, D. C., of which Dr. Francis G. Blake, Sterling professor of medicine, Yale University School of Medicine, New Haven, Conn., is chairman. A list of the candidates and institutions where they are to work follows:

Dr. Reginald M. Archibald, Toronto, Ont., Rockefeller Institute for Medical Research.

Dr. Frederik B. Bang, Baltimore, Vanderbilt University, Nashville, Tenn.

Dr. Lindsay A. Beaton, Chicago, Northwestern University, Chicago.

Dr. Albert H. Coons, Boston, Harvard Medical School, Boston.

Dr. Joseph Russell Elkinton, Philadelphia, Yale.

Dr. Hugh W. Garol, San Francisco, Yale.

Arden Howell Jr., Ph.D. (renewal), Duke University, Durham, N. C.

Dr. Carl A. Moyer, Ann Arbor, Mich., Massachusetts General Hospital, Boston.

Dr. Abe Ravin, Denver (renewal), Harvard.

Joseph Shack, Ph.D. (renewal), John Hopkins University, Baltimore.

Dr. William M. Wallace, Boston (renewal), Harvard.

Richard J. Wenzler, Ph.D. (renewal), Cornell University Medical College, New York.

Earl H. Wood, Ph.D., University of Pennsylvania, Philadelphia.

Special Society Elections.—Dr. William H. Guy, Pittsburgh, was elected president of the American Dermatological Society at the annual meeting in Colorado Springs in June. Dr. Harry R. Foerster, Milwaukee, is secretary. The 1941 meeting will be in New Orleans.—Dr. John L. Lattimore, Topeka, Kan., was made president-elect of the American Society of Clinical Pathologists at the annual meeting in New York in June. Dr. Armin V. St. George, New York, is president and Dr. Alfred S. Giordano, South Bend, Ind., is secretary. The 1941 meeting will be in Cleveland prior to the annual session of the American Medical Association.—Dr. Milton B. Cohen, Cleveland, was chosen president-elect of the American Society for the Study of Allergy at the annual meeting in New York, June 10-11, and Dr. Robert L. Benson, Portland, Ore., became president. Dr. Samuel M. Feinberg, Chicago, was elected vice president. Dr. James Harvey Black, Dallas, Texas, is secretary.—Dr. Benjamin Goldberg, Chicago, was named president-elect of the American College of Chest Physicians at the annual meeting in New York and Dr. John H. Peck, Oakdale, Iowa, was installed as president. Drs. J. Winthrop Peabody, Washington, D. C., and Mathew Jay Flipse, Miami, Fla., were elected vice presidents and Dr. Paul H. Holinger, Chicago, was elected secretary.

CANADA

Personal.—Dr. Alan Brown, professor of pediatrics, University of Toronto Faculty of Medicine, Toronto, has been made a fellow of the Royal College of Physicians of London (honoris causa).—Dr. Edward W. Archibald, emeritus professor of surgery, McGill University Faculty of Medicine, Montreal, and Dr. C. L. Pierre Masson, professor of pathological anatomy, University of Montreal Faculty of Medicine, received honorary degrees of doctor of science at the recent convocation of McGill University.

CORRECTIONS

Dr. Rea will Continue Teaching.—In *THE JOURNAL*, June 29, page 2576, it was reported that Dr. Charles E. Rea had resigned his position as assistant professor of surgery at the University of Minnesota Medical School to enter private practice in St. Paul. Dr. Rea writes that he resigned from full time teaching but will continue on a part time basis.

Paper Presented by Dr. Rieser.—In a news item in *THE JOURNAL*, July 6, page 65, reporting a district meeting in Georgia a paper on "Etiologic Factors of Human Sterility in the Male" was listed as having been given by Dr. Robert Norton, Rome, Ga. This should have been credited to Dr. Charles Rieser, Atlanta. Dr. Norton discussed the preceding paper on the program.

Intravenous Anesthesia.—Under the title "Intravenous Anesthesia" in *Queries and Minor Notes* in *THE JOURNAL*, July 6, page 73, in the last sentence of the first paragraph the word "cyanotic" should have been "burned." In the first sentence of the second paragraph the dose should have read "1 gram" (not "1 grain") and in the last sentence of the first paragraph also "1 gram" (not "1 grain").

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 22, 1940.

Improvement in Respirators for Use in Gas Attacks

So far the Germans appear to have made no use of their innovation of the last war—the use of poison gas. But we are taking no risks. Respirators have been issued to the troops and also to every civilian in the country. In these respirators activated carbon is the agent for the absorption of poisonous gases and there is a pad of wool and asbestos for the absorption of smokes, but this is evidently thought not to be quite sufficient. A new filter is therefore being added to the existing respirators to increase their efficiency against smokes. It is a shallow tin box which is affixed by adhesive tape to the millions of respirators already issued to the civilian population. The work is being done by the air raid wardens throughout the country. A description of the mode of action of the new filter has not been published.

The First Wartime Pharmacopeia

The first wartime addition to the British pharmacopeia, published under the direction of the General Medical Council, contains ten new monographs and amends five of those of the last pharmacopeia, which was published in 1932 and had an addendum in 1936. The principal change in the new publication, of which the official title is "Second Addition to the British Pharmacopeia, 1932" is cod liver oil substitute. Nine of the ten new monographs are due to the shortage of oil extracted from the cod's liver, which is a result of the war. Formulas are given for an emulsion containing 50 per cent of cod liver oil and for an "emulsion of vitaminized oil devised to be equivalent as regards vitamins to the emulsion of cod liver oil." It consists of vitamins A and D dissolved in peanut oil or other suitable vegetable oils. Alternatively it may consist of a suitable fish liver oil or blend of fish liver oils. The ninth monograph on oils containing vitamins deals with halibut liver oil, for which a standard is now laid down. The tenth new monograph gives a formula for tetanus toxoid. The five monographs which are amended deal with liniment of camphor hydrous ointment, compound ointment of mercury, ointment of capsicum and ointment of tannic acid.

Effect of the War on Drug Supplies

The Netherlands, the Netherlands colonies and Belgium are important sources of drugs used in all countries, the supply of which is now cut off or reduced. The most important drug to be affected is quinine, for its world market is controlled from Amsterdam and more than 95 per cent of the cinchona bark used in its production comes from the Netherlands island of Java. Fortunately it seems that ample reserves of the alkaloid are in the military stores of the Allies and sufficient for civilian needs are warehoused in England. The market for caffeine and theobromine is also dominated by Netherlands production; the former is extracted from tea and coffee waste and the latter from cocoa husk. A by-product of the manufacture of cocoa, cacao butter, is also an important commodity of Netherlands commerce. So also are the oils of caraway seed and nutmeg and gum benzoin, of which the tree *Styrax benzoin* grows in Sumatra. The best variety of aloes is produced in Netherlands islands. In Belgium many vegetable drugs, such as valerian and dandelion roots, marsh mallow and henbane, are cultivated. Since the war has placed obstacles in the way of trade in these substances from middle Europe, dealers have been able to satisfy some of their requirements by transferring orders to Belgium growers. Now of course this source also is affected.

Emergency Food Plans

The approach of the battlefield to our shores has led to new precautions. In a previous letter it was stated that the Ministry of Health had decentralized its administration by dividing the country into districts, each with its own center. This was done because of the possible effects of an attack on London from the air. A similar course has now been taken with regard to food, the distribution and sale of which has been controlled by the government since the outbreak of the war. In order to insure distribution in case of emergency, the country has been divided into seventeen food areas in which in time of crisis officers of the Ministry of Food will assume supreme control if communications break down. Beyond this there is a further division of the country into 800 self-supporting areas, each with its own depot. The minister of food, Lord Woolton, describes the scheme as a revolution in the dispersal of foodstuffs and one which should prevent people from seeking to store unduly large quantities of food in their homes. Each of the 800 little areas would have enough food for a few weeks without any help from the outside. In times of emergency there would be no long journeys with food supplies from the ports. The main roads would have to be kept as free as possible for military movements.

Control of Cerebrospinal Fever Among Troops

The War Office has issued a memorandum on the measures to be taken to control cerebrospinal fever among the troops. If a suspected case occurs, the medical officer must at once notify it and telephone or telegraph to the pathologist in charge of the laboratory allotted to the area and make arrangements for the isolation and treatment of the case and for isolation of contacts pending the arrival of the pathologist. For prevention, overcrowding must be avoided. In sleeping quarters there should be an interval of at least 6 feet between the centers of adjacent beds. In war this may not be possible and then at least 2½ feet must be maintained. If the distance is less than 3½ feet, every alternate bed must be turned round, so that each man sleeps with his head opposite his neighbor's feet.

For treatment, sulfanilamide or sulfapyridine is recommended. As a rule only one of these should be administered, but if there is intolerance, as shown by nausea, vomiting, depression or insomnia, a change to the other drug may cause the symptoms to disappear. The dosage should be sufficient to maintain in the cerebrospinal fluid a concentration of 5 mg. per hundred cubic centimeters for three days and a slightly lower one for a further five or six days. As long as these drugs are being administered, the intake of fluids should be about 4 pints (2 liters) daily so as to maintain a reasonable balance between blood concentration and urinary excretion. The total dose in the twenty-four hours should be 8 Gm., and in extreme cases a maximum of 10 Gm. Spacing is important. The drug should be given every four hours night and day. At the beginning half the twenty-four hour dose should be given in the first two doses. After this an equal dose should be given every four hours. After two and one-half to three days the dose over the next six days should be gradually reduced to 2 or 3 Gm. daily. To prevent recurrence the drug should be administered for some days after disappearance of the symptoms, but normally the total period need not exceed nine days.

The Prevention of Diphtheria

The Royal College of Physicians has passed a resolution urging the Ministry of Health to encourage the immunization against diphtheria of children in the age group 1-15 in view of the fact that there has been no abatement in the incidence or permanent reduction in the mortality since the early years of the century. The cost of prophylactics should not be allowed to interfere with schemes which would reduce the incidence of diphtheria. Where outbreaks occur, advantage should be taken of the Emergency Laboratory Service to help to control them.

The college also draws the attention of the ministry to the fact that children brought up on pasteurized milk in the towns have since their evacuation to the country, because of the danger of air raids, been receiving raw milk. Arrangements should be made to secure supplies of pasteurized milk in all areas where there are numbers of children to demand it. Further, physicians should advise parents of the risks of infection in consuming raw milk and the value of pasteurization or boiling in removing them.

ITALY

(From Our Regular Correspondent)

June 15, 1940.

Obligatory Vaccination Against Diphtheria

A recent law makes antidiphtheric vaccination obligatory for children between 2 and 10 years of age. Communities will have centers for free administration of the vaccines, which will be provided by the municipalities. The child's family can select the physician it wants for carrying on vaccination. Physicians will report vaccinations performed to the proper authorities in the department of hygiene in the community, who will register the report in a record book and send a certificate to the family through the physician. The certificate is to be shown when the child enters school. If the child has not been vaccinated against smallpox he is given anti-smallpox vaccination just before administration of the first antidiphtheric injection. The results of the anti-smallpox vaccination are controlled twenty-one days after administration of anti-smallpox vaccine and then the second antidiphtheric injection is done. Children provided with medical certificates showing that they have had diphtheria or that they suffer from asthma or from renal or cutaneous diseases are excluded by the law from obligatory antidiphtheric vaccination.

Medical Meeting

The Medical Society of Libya recently met in Tripoli. Professor Ciotola spoke on the epidemiology of exanthematic typhus and on the satisfactory results of vaccines, which are administered according to Weil's method for the prevention of the disease. Professor Casati reported satisfactory results with sulfanilamide in about 400 cases of conjunctivitis from streptococci with grave corneal complications. The drug produced rapid and lasting satisfactory results in corneal complications of trachoma and scanty results in conjunctivitis of the Koch-Weeks type. Drs. Nastasi and Azzarello reported satisfactory results from flying at altitudes of between 2,500 and 3,500 meters for children with whooping cough. The attacks of cough stopped immediately in 50 per cent of the cases. The speakers believe that a factor which up to now is unknown is present during flying at altitudes and that it assumes a special role on the nervous pathologic stimulation which causes cough. Dr. Bravi reviewed the literature on the treatment of epilepsy. He used dilantin sodium in the treatment of symptomatic epilepsy. He concluded that in grave forms of the disease the crises stop for the first thirty or forty-five days after administration of the treatment. Then they reappear at long intervals. In forms of moderate acuteness of the disease the crises seem to be controlled.

Operations and the Blood Pressure

Professor Bassi of Pavia, in a lecture recently delivered to the Accademia Medico-Chirurgica of that city, reported observations on forty patients who had operations under general ether anesthesia or else local procaine hydrochloride anesthesia. He determined the blood pressure before the operation and several times a day for the first ten days after the operation. The arterial blood pressure showed moderate upward oscillations in 50 per cent of the patients who had operations with general ether anesthesia and moderate downward oscillations in the remaining patients. In the larger number of patients who had local anesthesia the arterial blood pressure increased shortly

after the operation and diminished during the following days. The venous blood pressure diminished in the majority of cases in the whole group. Moderate lowering began a few hours after the operation and progressed during the following days. The venous blood pressure showed no relation to the variations of the pulse and the temperature. Often the pressure diminished in the presence of frequent respiration. The behavior of the venous blood pressure paralleled that of the arterial blood pressure in half the number of cases. The velocity of circulation showed moderate diminution in the majority of cases of general ether anesthesia. It moderately increased during the first few hours after local anesthesia and then it diminished for the following few days. The most observable alterations appeared within twenty to thirty hours after the operation. The speaker used the apparatus of Alestra and Ruffini for studying the behavior of the venous pressure and Hirschsolun and Maendl's method with calcium chloride for determining the velocity of circulation.

Congenital Malformation of Esophagus

Professor Cajano, in a lecture recently delivered to the Accademia delle Scienze Mediche e Chirurgiche of Naples, reported observations on congenital malformation of the esophagus in newborn infants, which were found in two cases out of a total number of 900 necropsies. There was atresia of the esophagus between the upper and middle thirds of the structure in both cases. Esophagotracheal fistula was present in one case and stenosis of the cardiac orifice in the other case. The speaker said that esophageal malformations are rare. The literature from 1670 to the present contains about 300 case reports. The most frequent type (80 per cent of the reported cases) consists of atresia of the esophagus and esophagotracheal fistula. The signs of esophageal atresia are characteristic. Seromucous liquid is constantly eliminated from the mouth, the attacks of suffocation are frequent and deglutition is impossible. The prognosis is poor. Not even surgery has succeeded. None of the theories on the etiology and pathogenesis of the condition are clear and precise. The theories more frequently given are those concerning early embryonal malformation with abnormal hyperdevelopment of the cardiac segment in the presence of abnormal blood vessels or else the persistence of physiologic epithelial occlusion at the esophagus. The speaker believes that the main factor is a primary deviation of embryonic development at the cephalic portion of the primary intestine, at which point the tracheo-esophageal segment develops. The cause of the deviation is unknown. The speaker carried on serial microscopic examinations of the atresic segment in his cases and found neither actual, local or general conditions in relation to the cause of atresia nor signs of any causing condition in the past.

Marriages

JOHN SAMUEL SLATE, Winston-Salem, N. C., to Miss Lora Mae La Foy of Anderson, S. C., May 18.

OLIVER EDMONDS TURNER, Pittsburgh, to Miss Dorothy Elizabeth Huber of Philadelphia, June 14.

VERNON W. TAYLOR JR., Oxford, N. C., to Miss Vida Grace Babb of Johnstown, Pa., June 1.

ERNEST FREDERICK BRIGHT, Cleveland, to Miss Elizabeth Thompson Morse of Boston, May 16.

WELDON TROEH ROSS, McMinnville, Ore., to Miss Waunita Luke of Holdredge, Neb., July 6.

ROBERT SHEARER HELLMANN to Miss Mary Catherine Elliott, both of Jackson, Tenn., June 8.

WILLIS W. BOWERS JR., Granite City, Ill., to Miss Lois Eddy of Kenton, Ohio, June 1.

WILLIAM EDWARD STOREY to Miss Virginia Johnson, both of Columbus, Ga., June 5.

JAMES THOMAS GREEN to Miss Mary Wright Shand, both of Columbia, S. C., June 4.

Deaths

Austin Albert Hayden ☉ Secretary of the Board of Trustees of the American Medical Association, a distinguished worker in the field of ophthalmology and otolaryngology, died in Chicago, July 10, of coronary thrombosis.

Dr. Hayden was born in Shullsburg, Wis., Oct. 15, 1881. His premedical education was received at Creighton University in Omaha and at the University of Chicago. He received his M.D. degree from Rush Medical College in 1904, served his internship in St. Elizabeth's Hospital and served also as intern in St. Anne's Hospital. He was instructor in ophthalmology and did graduate work at the New York Post-Graduate Medical School from 1906 to 1908, and then was instructor in ophthalmology at Rush from 1908 to 1916.

In his professional life Dr. Hayden was active in the work of many medical organizations. He was a fellow of the American College of Surgeons, a member of the American Otolological Society, a former president of the Chicago Laryngological and Otolological Society and of the Chicago Medical Society. He was also a member of the Chicago Ophthalmological Society, the American Academy of Ophthalmology and Otolaryngology, the American Laryngological, Rhinological and Otolological Society, a former president of the American Association of Railway Surgeons and a member of the Institute of Medicine and the Society of Medical History of Chicago.

In more recent years he had given much attention to the problems of those who are hard of hearing and had served as president of the Chicago League for the Hard of Hearing and of the American Federation of Organizations for the Hard of Hearing. He had also contributed greatly to the development of hearing devices and recently published contributions on this subject both in scientific periodicals and in such publications for the layman as *Hygeia* and the *Reader's Digest*.

In the American Medical Association Dr. Hayden had served as treasurer from 1922 to 1933 and since 1933 he had been Secretary of the Board of Trustees. He was devoted to his work for organized medicine, giving much of his time also to the recently organized National Physicians' Committee, of which he was secretary.

At the meeting of the American Medical Association just held in New York he worked many hours during the day and night in his official capacities not only on the Board of Trustees and in the work of the House of Delegates but also in charge of entertainment during the session. He became ill following his return from the meeting and had been almost constantly in the hospital since that date. Dr. Hayden was known to his friends for his intense activity, his constant courtesy, his genial friendship and particularly his leadership in medical advancement. The debt of organized medicine to men of his type who give so freely of themselves for the common good cannot be too greatly recognized.

Samuel Horton Brown ☉ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1899; member of the American Academy of Ophthalmology and Otolaryngology; formerly member of the State Council for the Blind; ophthalmologist to the Mount Sinai Hospital, St. Luke's and Children's Hospital and the American Hospital for Diseases of the Stomach; editor of the seventh, eighth and ninth editions, from 1904 to 1906, of "Hughes' Practice of Medicine"; associate editor of the "American Year Book of Medicine and Surgery," 1904-1905; author of "Eczema, Its Causes, Diagnosis and Treatment," published in 1906; author, with William C. Posey, of "History of Will's Hospital," published in 1931; editor of the *Weekly Roster and Medical Digest*, official organ of the Philadelphia County Medical Society; aged 61; died, June 12.



AUSTIN ALBERT HAYDEN, M.D.
1881-1940

Claude Thomas Uren ☉ Omaha; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1910; professor of otology and rhinology at the Creighton University School of Medicine; past president of the Omaha-Douglas County Medical Society; member of the American Academy of Ophthalmology and Oto-Laryngology; American Laryngological, Rhinological and Otolological Society and the American Otolological Society, Inc.; served during the World War; fellow of the American College of Surgeons; attending otolaryngologist to St. Joseph's and Douglas County hospitals; aged 52; died, May 16, of cerebral hemorrhage.

George Gray Sears, Boston; Harvard Medical School, Boston, 1885; member of the Massachusetts Medical Society and the Association of American Physicians; professor emeritus of clinical medicine at his alma mater and at various times instructor, assistant professor of clinical medicine, clinical professor and professor of clinical medicine; visiting physician, Boston City Hospital, from 1902 to 1919, trustee since 1918 and consulting physician since 1919; trustee of the Forsythe Dental Infirmary since 1924; vice president of the Boston Medical Library from 1928 to 1935; aged 80; died, May 28.

Martin William Peck, Boston; Harvard Medical School, Boston, 1915; for many years instructor of psychiatry at his alma mater; member of the American Psychoanalytic Association, American Psychiatric Association and the New England Society of Psychiatry; past president of the Boston Psychoanalytic Society; served during the World War; formerly on the staffs of the Massachusetts General Hospital and the Boston Psychopathic Hospital; author of "The Meaning of Psycho-Analysis"; a trustee of the Boston Psychoanalytic Institute; aged 59, died, May 7, of a self-inflicted bullet wound.

Hunter Robb, Burlington, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1884; associate in gynecology at the Johns Hopkins University School of Medicine, Baltimore, from 1889 to 1894; formerly professor of gynecology at the Western Reserve University School of Medicine, Cleveland; at one time visiting gynecologist to the Lakeside Hospital, Cleveland; fellow of the American College of Surgeons; served during the World War; author of "Aseptic Surgical Technique," published in 1894; aged 76; died, May 15, of pneumonia.

William Harvey Smith, Winnipeg, Man., Canada; McGill University Faculty of Medicine, Montreal, Que., 1892; professor emeritus of ophthalmology at the University of Manitoba Faculty of Medicine; past president of the British Medical Association, Canadian Medical Association, Manitoba Medical Association, College of Physicians and Surgeons of Manitoba and the Winnipeg Medical Society; fellow of the American College of Surgeons; honorary consultant, Winnipeg General Hospital; aged 71; died, May 15, of carcinoma of the prostate.

William Reginald Leonard Hathaway, Milo, Maine; Medical School of Maine, Portland, 1901; member of the Maine Medical Association; past president of the Piscataquis County Medical Society; for many years member of the school board of Milo and school physician; formerly member of the state house of representatives and state senate; aged 62; died, May 26, of chronic nephritis and hypertensive heart disease.

Baldwin Mann, Collins, N. Y.; Johns Hopkins University School of Medicine, Baltimore, 1909; formerly assistant professor of medicine and therapeutics at the University of Buffalo School of Medicine; past president of the Medical Society of the County of Erie; served during the World War; at one time on the staff of the Buffalo General Hospital; aged 57; died, May 9, in Canandaigua.

Summerfield Moon Taylor, Austin, Texas; University of Texas School of Medicine, Galveston, 1913; member of the State Medical Association of Texas; fellow of the American College of Surgeons; on the staffs of the Seton Infirmary, Brackenridge Hospital and St. David's Hospital and the Texas Deaf, Dumb and Blind Institute; aged 50; died, May 27, of coronary artery occlusion.

Charles Julius Plonske ☉ Faribault, Minn.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; president of the Rice County Medical Society; on the staffs of St. Lucas Evangelical Deaconess Hospital and the Minnesota School for Feeble-minded; aged 69; died, May 16, of carcinoma of the lung with metastasis to the cerebrum.

Forrest Foster Slyfield, Duluth, Minn.; Rush Medical College, Chicago, 1911; member of the Minnesota State Medical Association; on the staffs of the Miller Memorial Hospital, Webber Hospital, St. Luke's Hospital and St. Mary's Hospital; aged 53; died, May 2, of coronary thrombosis.

David Becker Pindar, Hoboken, N. J.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1889; formerly member of the city board of health; school physician; for many years on the staff of St. Mary's Hospital; aged 74; died, May 5, of septicemia.

Charles Espy Mordoff, Oakland, Calif.; College of Physicians and Surgeons, Los Angeles, 1910; member of the California Medical Association; served during the World War; aged 56; died, May 7, in the Providence Hospital of cerebral hemorrhage, myocarditis and hypertension.

Charles Homer Bair @ Wilmerding, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1904; public school physician and president of the board of health; aged 64; died, May 20, in the Western Pennsylvania Hospital, Pittsburgh, of chronic nephritis and acute cholecystitis.

Clarence Nicholas Sonnenburg, Sheboygan, Wis.; Marquette University School of Medicine, Milwaukee, 1915; member of the State Medical Society of Wisconsin; served during the World War; formerly county coroner; aged 48; died, May 5, in St. Nicholas Hospital.

Daniel Irwin Jamison, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1897; member of the Medical Society of the State of Pennsylvania; aged 70; died, May 17, in the Shadyside Hospital of mesenteric thrombosis and lobar pneumonia.

Tubal J. Ziegler, Richmond Hill, N. Y.; Cincinnati College of Medicine and Surgery, 1887; at one time adjunct professor to the chair of materia medica and therapeutics at the Chattanooga (Tenn.) Medical College; aged 82; died, May 27, of coronary thrombosis.

Bergen Fred Illston, Utica, N. Y.; University of Buffalo School of Medicine, 1901; served during the World War; formerly coroner of Jamestown; aged 61; died, May 15, in the Veterans Administration Facility, Batavia, of carcinoma of the colon.

Eva Charlotte Reid, San Francisco; Cornell University Medical College, New York, 1907; formerly associate clinical professor of psychiatry at the University of California Medical School; served during the World War; aged 66; died, May 1.

Isidore Daniel Haskell, Newark, N. J.; Vanderbilt University School of Medicine, Nashville, Tenn., 1912; served during the World War; aged 53; died, May 25, in the Beth Israel Hospital of arteriosclerosis and heart disease.

Bert Lee Stollar @ Fayette City, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1906; served during the World War; aged 56; died, May 5, in the Mercy Hospital, Pittsburgh, of acute staphylococcal endocarditis.

John Read, Los Angeles; University of Pennsylvania Department of Medicine, Philadelphia, 1904; member of the Medical Society of the State of Pennsylvania; aged 60; died, May 2, in Glendale, Calif., of bronchial asthma.

Henry Ernest Chaput, Chicopee Falls, Mass.; School of Medicine and Surgery of Montreal, 1894; aged 70; died, May 4, in the Women's Homeopathic Hospital, Philadelphia, of hypertrophy of the prostate and cardiorenal disease.

Herbert Ausburn Rodenbaugh, Barberton, Ohio; Ohio Medical University, Columbus, 1902; member of the Ohio State Medical Association; served during the World War; aged 65; died, May 27, of acute myocarditis.

Herbert Waldo Emsheimer, Los Angeles; Columbia University College of Physicians and Surgeons, New York, 1909; served during the World War; on the staff of the Cedars of Lebanon Hospital; aged 54; died, May 20.

Murray Elliott Ramsey, Westfield, N. J.; Medical College of Ohio, Cincinnati, 1889; formerly member of the board of education; aged 72; died, May 9, in the Muhlenberg Hospital, Plainfield, of arteriosclerosis and nephritis.

James Allen Rhodes, Horn Lake, Miss.; Memphis (Tenn.) Hospital Medical College, 1911; member of the Mississippi State Medical Association; for many years postmaster; aged 68; died, May 31, of cirrhosis of the liver.

John Gerard Sweeney, Hingham, Mass.; Tufts College Medical School, Boston, 1916; formerly medical examiner of the fifth Plymouth district; aged 45; was found dead, May 18, of a skull fracture received in a fall.

William C. Raughley @ Berlin, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1884; aged 75; died, May 11, in the Cooper Hospital, Camden, of posterior coronary artery occlusion.

John Shields-Taugher, Waukesha, Wis.; Marquette University School of Medicine, Milwaukee, 1933; member of the State Medical Society of Wisconsin; aged 33; died, May 18, in an automobile accident.

William Allen Raiman @ Swarthmore, Pa.; Medico-Chirurgical College of Philadelphia, 1905; aged 60; died, May 18, in the Temple University Hospital, Philadelphia, of diverticulosis and peritonitis.

Thomas Jacob Coble, Shelbyville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1898; member of the Tennessee State Medical Association; aged 69; died, May 19, of coronary thrombosis.

James V. May, Port Gibson, Miss.; Louisville (Ky.) Medical College, 1903; member of the Mississippi State Medical Association; aged 64; died, May 9, of chronic myocarditis and adhesive pericarditis.

Henry Osborn Carhart, Blairstown, N. J.; Jefferson Medical College of Philadelphia, 1886; medical examiner for the state highway department; formerly state senator; aged 76; died, May 22.

John S. Yates @ Rosenberg, Texas; University of Texas School of Medicine, Galveston, 1903; on the staff of the Fort Bend Hospital; aged 64; died, April 6, of heart disease and chronic nephritis.

Percy Lee Hamilton @ Chico, Calif.; California Medical College, San Francisco, 1896; past president of the Butte County Medical Society; aged 65; died, May 9, of carcinoma of the rectum.

James Crittington Parrott, Natchitoches, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1903; member of the Louisiana State Medical Society; aged 66; died, May 16, of coronary thrombosis.

August Friederick Gustav Paetzel, Sharon, Pa.; Maryland Medical College, Baltimore, 1907; aged 68; died, May 31, in a hospital at Mercer, of cerebral hemorrhage and chronic myocarditis.

Benjamin F. Rynerson, Prairieton, Ind.; University of Louisville (Ky.) Medical Department, 1888; aged 82; died, May 13, in the Union Hospital, Terre Haute, of chronic nephritis.

Fred Merritt Stiles, Waltham, Mass.; Medical School of Maine, Portland, 1890; member of the Massachusetts Medical Society; aged 76; died, May 10, of acute coronary thrombosis.

John Cleveland Luster, Davis, Okla.; Keokuk (Iowa) Medical College, 1898; member of the Oklahoma State Medical Association; aged 64; died, May 17, of heart disease.

Emily Jane Ingram Stephens, Telford, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1883; aged 83; died, May 26, in the Grand View Hospital, Sellersville.

Benjamin Stetson, Oakland, Calif.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1890; aged 79; died, May 22, of coronary occlusion and chronic myocarditis.

William Henry Pennington, Mineral Wells, Texas; Missouri Medical College, St. Louis, 1876; aged 84; died, May 9, in the Nazareth Hospital of diabetic acidosis.

Jefferson D. Hammett, Huntsville, Mo.; University of Pennsylvania Department of Medicine, Philadelphia, 1870; aged 92; died, May 12, of chronic myocarditis.

Charles Marion Tinney, Los Angeles; Kansas City Medical College, 1900; served during the World War; aged 60; died, May 18, in the California Lutheran Hospital.

John Henry Bell, Hamilton, Ont., Canada; Trinity Medical College, Toronto, and Queen's University Faculty of Medicine, Kingston, 1890; aged 73; died, May 8.

Columbus H. McCuistion, Valley View, Texas; American Medical College, St. Louis, 1899; aged 77; died, May 16, of coronary heart disease.

William H. Thompson @ Winterset, Iowa; Jefferson Medical College of Philadelphia, 1884; aged 83; died, May 16, of cerebral thrombosis.

George Bigler Ehrman, Miami Beach, Fla.; Pulte Medical College, Cincinnati, 1883; aged 81; died, May 23, of pneumonia and uremia.

Irwin McMurchie Lloyd, Sault Ste Marie, Ont., Canada; University of Toronto Faculty of Medicine, 1918; aged 43; died, May 9.

Benjamin F. P. Johnston, Rosebush, Mich.; Detroit College of Medicine, 1895; aged 68; died, May 31, of coronary thrombosis.

Bureau of Investigation

A "HAIR COLOR RESTORER" AND A "HAIR GROWER" FOUND FRAUDULENT

Dermo-Cosmetic Products Co. Debarred from the Mails

"Hair color restorers" were widely advertised until the Food and Drug Administration, which enforces the Food, Drug and Cosmetic Act, notified manufacturers of such products that this designation would be considered under the act as false and misleading. Most such color restorers apparently were sold at cosmetic counters rather than through the mails. Within the past year, however, the Post Office Department has closed the mails to a New York concern that put out such a product along with a "dandruff lotion."

According to the memorandum prepared on this case by Hon. Vincent M. Miles, Solicitor for the department, the firm in question did business under the names Dermo Co. and Dermo-Cosmetic Products Co. The business was run by a Joseph Kesler and his wife, Anne Kesler, apparently also known as Anne Kaye. They advertised in various publications, puffing the alleged powers of their "Grey-X" and "Hair-Giene."

Some of the advertisements for Grey-X did not mention the product by name—for example:

GRAY HAIR disappears gradually, natural looking effect; money back guarantee. Priced by thousands, \$1.00 bottle. Free Booklet. DERMO CO., Dept. G. S. 1465 Bway, N. Y. C.

Those who wrote for particulars received circulars containing such preposterous claims as:

Natural Color RESTORED (Does NOT dye the hair) . . . A Sure Preparation to Restore Gray Hair to Its Original, Natural Color. Science now proclaims that YOUR HAIR NEVER NEED BE GRAY. This wonderful new preparation imparts to grey or white hair, a perfectly natural color from light blonde to the most intense black. . . LOOK 15 TO 20 YEARS YOUNGER IMMEDIATELY—Youth and Beauty RESTORED. A TONIC—NOT A DYE. Good for Hair and Scalp. Effective against Dandruff and other Skin Irritations. Guaranteed to restore original color. Equally effective for men and women. . . GREY-X, the new and positive treatment for gray hair. . . You can hold on to youth and beauty with GREY-X. The transformation is so complete, perfect and natural appearing that your most intimate friends will never detect the use of GREY-X. . . It is so different. Remember, this preparation GREY-X is not like a quick acting hair dye. You use it like a hair tonic.

Statements made by the promoters of Grey-X to the Post Office Inspector in this case and substantiated by analysis made by government chemists revealed that Grey-X was a mixture of lead acetate, sulfur, glycerin, rose water, distilled water and perfume. Judge Miles's memorandum pointed out that, despite the promoters' representation that Grey-X "does not 'dye' the hair," expert medical evidence showed that it was, in fact, "an ordinary artificial dye of the slow-acting type" and would not "restore grey or white hair to its 'natural' color as claimed" but would "merely dye it a dull, metallic and unnatural black, the intensity of the shade varying slightly in accordance with the amount of the product applied." The expert evidence further brought out "that the lead acetate contained in the preparation may be absorbed in the sebaceous glands of the scalp with dangerous results to the user."

Apparently this concern's other product, "Hair-Giene," also was advertised without mention of its name, as follows:

HAIR TROUBLE-DANDRUFF Write for Free booklet HC endorsed by physician tells how to correct and relieve all scalp conditions; dandruff, patchy baldness, etc. Dermo Co., 1465 Broadway N. Y. C.

Those who answered the advertisement received circulars reading in part:

YOUR HAIR WILL GROW IF TREATED PROPERLY. "HAIR-GIENE" THE ANTISEPTIC LOTION For the HAIR & SCALP Ends Dandruff Worries! Checks Excessive Falling Hair. Promotes the Growth of New Hair. . . This wonderful hair and scalp lotion is the result of many years of research and experimentation. It has been used successfully and exclusively by one of the leading Hair and Scalp institutions in New York City on thousands of men and women. Now, for the first time it is being offered direct to the public for aid in correcting local hair and scalp disorders such as dandruff, excessive falling hair, itching scalp and patchy baldness. "HAIR-GIENE" is antiseptic dry, stimulating and a fine scalp conditioner and hair dressing for in action, stimulating and a fine scalp conditioner and hair dressing for men and women. . . It is the ideal all purpose hair and scalp lotion—

for the correction and treatment of all local hair and scalp disorders. It is absolutely different than any hair and scalp products in the country. Contains NO ALCOHOL or any injurious ingredients.

Information from the company itself, supplemented by the work of the government chemists, brought out that the ingredients of Hair-Giene were salicylic acid, sulfur, quinine hydrochloride, tinctures of pilocarpine, mullein and cantharides, olive oil, shale oil, "perfumed oil," thymol, iodine and water.

The Solicitor's memorandum on this case commented in part that expert medical evidence showed that, although Hair-Giene when used as directed would act as a counterirritant, rubefacient and lubricant and might bring about a temporarily increased flow of blood to the normal scalp, it could not cause a supply of blood to reach the obstructed papillae; and that in some cases, where the blood vessels are not completely obstructed or the papillae altogether atrophied the preparation may produce the growth of down or "fuzz" that cannot be considered normal hair. The medical evidence also showed that though in lubricating the scalp Hair-Giene might tend to relieve itching due to dryness it would not overcome other causes of itching scalp such as ringworm or eczema but instead might add to the deposit of "scruff" and increase any infection present.

For these reasons and the misrepresentations made concerning Grey-X the evidence was declared to show that the promotion of this business was a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises, and on Sept. 22, 1939, a fraud order was issued against Dermo Co., Dermo-Cosmetic Products Co., Dermo Cosmetic Products Co., Joseph Kesler, Manager, Anne Kay, and their officers and agents as such, at New York.

It is interesting to note that another government agency, the Federal Trade Commission, also had taken action against this business. On April 29, 1939, the Commission announced that "Anne Kesler, formerly trading as Dermo-Cosmetic Products Co., and Joseph Kesler, her agent, and present owner of preparation designated 'Grey-X'" had agreed "to cease representing that use of their product will permanently restore gray hair to its natural color, keep the scalp healthy, eradicate dandruff, or promote the growth of hair. They also agree to cease representing that the product is a French discovery, is not a dye, and to discontinue otherwise making any misleading or untrue statement as to its composition."

Since three federal agencies have objected, either specifically or generally, to naming such products "hair color restorers," it should be self evident that in future promotions such items should be called hair dyes!

VARIOUS "SEX" FRAUDS—II

In the past year the Post Office Department has closed the mails to additional frauds of the sexual type. These frauds make their appeal to a class of individuals lacking in ordinary intelligence. Some of them appeal only to the feeble-minded or at least completely unintelligent individuals, while others, including impotence "cures," have a wider, but only slightly higher class, clientele.

For these reasons the Bureau of Investigation is publishing only the briefest outline of Post Office fraud orders of this type which have appeared in the last year or so.

These are named in the following list with the number designation of the fraud order, the date of issuance, the name of the product and its promoters, with its description, and a list of ingredients, if known:

No. 13622, Dec. 6, 1939, (name of treatment not reported); F. J. Schreiber, Pittsburg, Kan.; blue pellets for "youthful pep": phosphates, sulfates, chlorides of sodium and potassium; small amounts of zinc and iron; petrolatum (0.044 Gm.) and strychnine and yohimbine (0.0015 Gm.) per tablet; white tablets for "prostate sufferers": methenamine (5.18 grains per tablet) with a little starch.

No. 13625, Dec. 27, 1939, "Vigotabs," Dee Company, Chicago; for sexual weakness: essentially damiana, with zinc phosphide (one-twelfth grain), strychnine (0.023 grain) and anhydrous ferric oxide (one-twelfth grain) per tablet; "Bladotabs" (Dee Company, Chicago), for kidney and bladder troubles: plant material including cubeba, sandalwood, cayenne, Venice turpentine and one-twentieth grain of exsiccated ferrous sulfate per tablet.

No. 13631, Dec. 29, 1939, "Vita-Male"; The Mason Products Company of California and The Mason Laboratories of California, Los Angeles; for sexual debility, sterility, glandular disturbances and some other things;

in each tablet 7 grains of seaweed, which contains small amounts of iodine, sodium potassium, calcium, magnesium, iron, sulfur, chlorine and phosphorus.

No. 13689, Jan. 19, 1940, "Jermol Perles"; Interstate Health Products, New York; claiming that loss of reproductive powers, premature old age, abortion in females, suckling paralysis in infants, improper development of boys and girls, and lowered vitality [loss of] "zest," "zip" and "pep" are due solely to vitamin E deficiency, and that their product which contained wheat germ oil would relieve these conditions; 2 minims of wheat germ oil to each "perle."

No. 14171, May 27, 1940, "Glandex"; L. H. Paul and Hollywood Hygienic Products, Hollywood, Calif.; "sex rejuvenator"; in each tablet about one-sixth grain of thyroid, a "considerable amount" of protein, and "a very small amount" of iodine, with calcium oxide and phosphate. Paul previously had put out an essentially similar product, operating as "Vitalife Laboratory" and other titles, which business he had promised the Post Office to discontinue, whereas he appears simply to have changed the trade style under which he carried on his activities in this field.

[On June 10, 1937, another government agency, the Federal Trade Commission, announced that it had got the Hollywood Hygienic Products, Inc., to promise to discontinue representing that its "Glandex" was a tonic and competent remedy for nervousness and sleeplessness; that its "Hollywood Dainties" had "germicidal qualities" which "become active at once"; that its "Ur-Gard" was a medical corps prophylactic effective for prevention or treatment of social diseases generally, and that its "Retardex" was a gland tonic, was harmless, and had been used with success where other remedies had failed.]

Correspondence

GALLSTONES IN CHILDREN

To the Editor:—The excellent article by Seidler and Brakeley on "Gallstones in Children" (*THE JOURNAL*, May 25, p. 2082) fails to mention, in consideration of etiology, the importance of hemolytic anemia. The bouts of excessive bilirubinemia and pigment excretion characteristic of certain cases of congenital hemolytic ictero-anemia and of sickle cell anemia seem to predispose to early gallstone formation. In the past few years I have seen two examples of each condition in patients under 15 years of age. The following synopsis of the history of a recent case will serve to illustrate the point:

A lad of 14 was referred because the family physician was unwilling to accept the diagnosis and hopeless prognosis, given elsewhere, of "terminal juvenile biliary cirrhosis." Examination disclosed deep jaundice, mahogany colored urine, fever, a mass in the liver area, splenomegaly, dehydration, purpura and ominous drowsiness. The boy had been "sickly" for five or six years but had "kept going" until two weeks before I saw him, when acute abdominal distress and deep jaundice supervened. Laboratory studies showed a putty colored acholic stool, marked bilirubinuria, an immediate direct van den Bergh reaction with "over 40 units" indirect, moderate anemia with 10 per cent reticulocytes, typical spherocytosis and a fragility test indicating hemolysis beginning at 0.650 and being complete at 0.425. A diagnosis was made of cholelithiasis with common duct stone complicating chronic hemolytic ictero-anemia. After preparation with vitamin K and a blood transfusion, which brought the prothrombin time from 128 seconds to twenty-four seconds, an operation was performed (Dr. I. S. Ravdin). Stones were removed from the distended gallbladder and common duct. Some weeks later, with subsidence of most of the jaundice but with increasing anemia and reticulocytosis and urobilinuria, the greatly enlarged spleen was removed. The boy made a splendid recovery, gained 18 pounds (8.2 Kg.) in two months and is perfectly well.

To complete this aspect of the problem of "gallstones in childhood," two additional points should be made: these hemolytic anemias, while predisposing to cholelithiasis, may produce bouts of abdominal pain independently of gallstones: the finding of gallstones in childhood suggests the advisability of careful hematologic study to establish or exclude the sometimes remarkably latent stigmas of hemolytic ictero-anemia.

THOMAS FITZ-HUGH JR., M.D., Philadelphia.

EDUCATION ABOUT DIABETES

To the Editor:—I have just read with interest your editorial on diabetes in Pennsylvania and am glad that you emphasize the importance of this disease as a public health problem.

Beginning about 1929, I have again and again called attention to the fact that here was one prevalent disease of later life for which medical science could do much, and that it was the responsibility of the health authorities to assume some leadership by carrying on the necessary educational work among both the general public and the medical profession. I finally induced Dr. Shirley Wynne, at that time city health commissioner, to take the matter up with the New York Academy of Medicine. A special committee, of which Dr. Mosenthal was chairman and of which I was a member, presented a report and this in turn subsequently led to the organization of the New York Diabetes Association. Dr. Ralph Scott is now president of the association and I am vice president.

That the registered death rate of diabetes has increased since the introduction of insulin is due almost entirely to the publicity given to the disease as the result of Banting's discovery. More and more diabetic patients are coming under the care of physicians, and more and more frequently is the diagnosis of diabetes being made. Routine testing of urines for sugar is also becoming more common.

Following New York City's lead, diabetes associations were established in Philadelphia, Cincinnati, Detroit, and Rochester, N. Y. In other parts of the country also there is beginning to be a realization of the importance of attacking diabetes as a public health problem. At the Atlantic City session of the American Medical Association in 1935 I had a booth giving pertinent statistical and other data and outlining a practicable control program. The latest issue of the *New York State Journal of Medicine* carries an article by Dr. Frederick Williams on the free summer camp maintained by the New York Diabetes Association for indigent New York diabetic children.

CHARLES F. BOLDUAN, M.D., New York.

Director, Bureau of Health Education.

A NOTE ON HISTAMINASE

To the Editor:—A recent communication to *THE JOURNAL* by Keeney on the treatment of hay fever by the oral administration of histaminase may possibly convey the impression that we have been in part responsible for the clinical use of this enzyme. The same impression could be secured from other reports and from the advertising material of the Winthrop Chemical Company.

In a review on histamine published by us in 1931 work on histaminase was summarized, and it was pointed out that the presence of the enzyme in various tissues, particularly the kidney, may constitute one of several defense mechanisms possessed by the body for the inactivation of histamine. It was not suggested, nor has this been done in any subsequent publication, that the administration of histaminase might be a useful mode of therapy.

Investigations in this laboratory in the period 1930-1932 showed that administration of histamine to animals for a period of some weeks has no effect on the histaminase content of the kidneys. It would be expected that increased need for histaminase would cause an increased production of the enzyme, especially during a prolonged period. A decrease in enzyme content is not observed after a single large dose of histamine. Protection of guinea pigs against anaphylactic and histamine shocks was attempted with completely negative results. After the publication of a paper on this subject by Brown and Karady the work was repeated and negative results were again secured.

It was reported in 1930 that histaminase was inactivated in acid solutions. This would suggest that introduction of the

enzyme into the stomach would render it inert. We have found, as would be expected, that histaminase is inactivated by pepsin in acid solution and by trypsin in slightly alkaline solution. It would be difficult to suppose that histaminase, given orally, could survive the action of proteolytic enzymes in the gastrointestinal tract. The suggestion might be made that histaminase, given orally, would inactivate histamine in the intestine, thus preventing the absorption of a toxic amine. It is most unlikely that such would occur, since the enzyme is itself rapidly destroyed by the digestive ferments.

Our investigations over a period of ten years have failed to show that the intravenous or intramuscular administration of histaminase has any effect on histamine present in the body or on that given by injection. Preparations of histaminase at least four times as potent as any commercially available have been used without success. Possibly very active enzyme preparations might have a demonstrable effect, but such preparations are not yet available.

The work on histaminase provided evidence regarding one of several mechanisms possessed by the body for the destruction of histamine. Data regarding the chemical and physical properties of the enzyme system were made available. The results of investigations which we considered to have no obvious practical application have been applied by others to clinical problems. For some years we have consistently answered numerous inquiries about histaminase with the statement that we believed there was no physiologic basis on which to rest its clinical use.

C. H. BEST, M.D.

E. W. McHENRY, PH.D., Toronto.

Department of Physiological Hygiene,
University of Toronto.

PULMONARY EMBOLISM FOLLOWING INJECTION TREATMENT OF VARICOSE VEINS

To the Editor:—The recent article of Dean and Dulin entitled "Pulmonary Embolism Following the Injection Treatment of Varicose Veins" (*THE JOURNAL*, April 6, p. 1344) has evoked two critical communications (*May 25*, p. 2139, and *June 22*, p. 2489). Tending to agree in substance with Dean and Dulin's thesis and to disagree with some of the criticisms, I wish to point out several facts.

The treatment of varicose veins is divided between surgeons on the one hand and dermatologists and general practitioners on the other. It is often pointedly odd that the former, who can do either an injection or an operation, will use both methods, depending on the type of case under treatment, while the latter, with a limited repertoire, will use only the method at hand. This, of course, does not apply to dermatologists with the standing and the facilities for referring cases of Dr. Isaak but is true of some medical men in smaller communities. Whereas the surgeon may prefer one type of treatment, he at least has a free choice. Those who are not surgeons must either inject or give up the case.

Another point concerning the treatment of veins is that case mortality must not be confused with treatment mortality. In a large series observed by Sicard and Gaugier, the average patient received eight injections. Thus, if a patient survives one injection he still has to receive the other seven on the average before his final mortality rate can be computed, and by this time the mortality rate per case approaches that for ligation as given in the literature. It is quite true, however, that the statistics of Westerborn, quoted by Isaak, do refer to patients, but this objection does not hold for some other statistics in the literature.

Isaak further quotes Kilbourne as stating concerning ligation: "Ligation may cause a funnel-shaped blind pocket in the vein proximal to the ligature" which may develop a thrombosis. It is to be pointed out that one of the chief purposes of the modern high ligation operation is to avoid this very funnel.

Another factor not sufficiently stressed in the literature is the beneficial effect of ambulatory treatment. Injections have almost always been done on ambulatory patients and hence have had the advantage of this factor with its accompanying low mortality. Ligations, on the other hand, have only recently been done almost entirely on ambulatory patients. In the literature little differentiation is made between mortality following ligation on bed and on ambulatory patients. If this is such an important factor, it would be only fair to compare the results of injection and ligation on only ambulatory patients. I myself am not aware of any death of an ambulatory ligation patient. So convinced am I of the importance of this feature of the treatment that I emphasize night walks as well as day exercise in the postoperative care. Patients are instructed never to stay in a bed longer than seven consecutive hours during the first two weeks after ligation. If they prefer to go to bed early and arise late, they must get up once or more during the night for a brief turn about the room. Patients are never operated on for varicose veins at the same time that other surgical procedures are performed or at a time when for any other reason they are likely to be kept in bed.

These points seem to me to answer several of the objections raised by Isaak in his criticism of Dean and Dulin's article. Finally, with regard to Taylor's communication stating that in one of two cases of pulmonary embolism reported by Dean and Dulin (following injection), since death occurred only after a second embolism, prophylactic ligation of the femoral vein should have been done after the first attack of embolism, I can only say that I disagree. It would seem far safer and less radical, and possibly even surer, to start heparin administration as advised by McClure and Lam in the same issue of *THE JOURNAL* as that in which Isaak's communication appeared.

HENRY N. HARKINS, M.D., PH.D.,
Henry Ford Hospital, Detroit

SYPHILIS CASE FINDING IN INDUSTRY

To the Editor:—In my article entitled "Syphilis Case Finding in Industry," published in *THE JOURNAL* April 6, an error was made in stating the annual attack rate of syphilis per hundred thousand of population in Great Britain. The statement in error appears in the fourth paragraph (p. 1321) and reads as follows: "The annual attack rate of syphilis per hundred thousand of population in the United States in 1935 was 796 compared with 47 in Great Britain (clinics only) . . ."

The correct annual attack rate of syphilis for Great Britain (England, Scotland and Wales) in 1935 was 15.3 per hundred thousand of population. It is, therefore, respectfully requested that a public correction notice be inserted in an early issue of *THE JOURNAL*. This notice should state that, through inadvertence, I incorrectly quoted an annual syphilis attack rate of 47 per hundred thousand of population for Great Britain in 1935 instead of a rate of 15.3 per hundred thousand. The rate of 47 per hundred thousand quoted in my article refers to the "number of cases dealt with for the first time at treatment centers" for syphilis. Since this figure includes patients with syphilis in all stages and patients who may have previously obtained treatment for syphilis through private physicians, the figure does not represent a true incidence rate.

ALBERT E. RUSSELL, M.D., Chicago.
Surgeon in Charge, Syphilis Control in Industry,
U. S. Public Health Service.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TREATMENT OF CHRONIC MALARIA

To the Editor:—A woman whose past history is essentially irrelevant had a repair of the cervix and pelvic laparotomy in 1933, when 42 years old. Her recovery was uneventful. Several months later she had an attack of fever and malaise which was diagnosed as malaria, and since she was allergic to quinine she was given fifteen $1\frac{1}{2}$ grain (0.1 Gm.) atabrine tablets. Her response was favorable and described by her as remarkable. Six weeks later she had a recurrence of fever and the same treatment was repeated. Since 1933 she has taken a course of atabrine every four to six weeks with several courses of plasmodochin following. She states that only during the time she is taking atabrine and for a few weeks afterward does she feel well. If there is a lapse of more than six weeks between courses she complains of nervousness, lassitude, low grade fever and weakness with a number of occasions when she is unable to get out of bed alone. As soon as she begins taking atabrine again she feels better and able to do about as she desires. She has taken from seventy to eighty courses of atabrine since 1933. To date I have been unable to find any harm caused by the treatment, which has been taken in spite of advice to the contrary given her by various physicians. She is intelligent and apparently not of a neurotic type. She states that only as a last resort has she at any time taken atabrine. Examinations by several competent internists have revealed only a mild secondary anemia. Her examinations include numerous blood smears and blood chemistry examinations, Widal tests and other agglutination tests and gastrointestinal x-ray studies, all of which are negative. At present except for a mild secondary anemia and a transient hypertension with the blood pressure varying from 120 systolic, 60 diastolic to 150/80, nothing significant has been found. The basal metabolic rate is -9 per cent. The following questions arise: Is this simply a neurosis? Can atabrine favorably influence any condition except malaria? Is it possible that this drug may act as a stimulant and by its slow elimination make the woman have a sense of well being until the drug is eliminated? Can the drug be habit forming? Surely, malaria can be eliminated.

M.D., Florida.

ANSWER:—An analysis of this case history suggests that a residuum of the infection is being maintained in spite of repeated courses of atabrine. Following the termination of a therapeutic course of atabrine (three $1\frac{1}{2}$ grain tablets a day for five days) a period of approximately a month is required before this drug is completely eliminated from the system. During this period probably all the parasites in the circulating blood are destroyed by the drug and the infection is kept at a subclinical level. It is even possible that the residual exo-erythrocytic plasmodia may be temporarily stupefied by the action of the drug. However, as soon as atabrine is completely eliminated the plasmodia again get into the circulating erythrocytes and multiply, with resulting clinical manifestations.

The statement that "surely, malaria can be eliminated" is probably true for most patients who are given adequate drugs at the beginning of the patent infection, and some patients probably become free from the plasmodia even without the benefit of antimalarial treatment. However, the consensus among malariologists today suggests that none of the known therapeutic agents alone or in combination can be guaranteed to eliminate the malaria plasmodia from the body unless the macrophage system actively cooperates in the attack. Thus, if the patient's resistance is low at the time of the initial attack or becomes lowered by repeated attacks, antimalarials alone can be expected to do no more than reduce the infection temporarily below clinical grade.

European malariologists are more and more recognizing the Ascoli technic as an important adjuvant in the treatment of chronic malaria. This consists of daily injections of epinephrine by the intravenous route. The first injection consists of 1 cc. of a 1:100,000 solution, the second 1 cc. of a 1:90,000 solution, the third 1 cc. of a 1:80,000 solution and so on daily until a strength of 1:10,000 has been reached. This last dose is repeated daily for approximately three weeks. In case intolerance develops to the stronger solutions, return may be made to a weaker solution and a second build-up attempted. The rationale of this technic is to throw the parasites out of the spleen into the circulation, so that they may then be attacked and killed by antimalarial drugs.

Treatment of chronic malaria is not the simple task it was believed to be even a decade ago. Hand in hand with antimalarial treatment there should be a program to build up the patient's resistance with rest and light exercise, vitamin therapy and relief from worry.

There is no evidence in the case cited that the patient is suffering primarily from a neurosis. Apparently she tolerates

atabrine extremely well. The only specific action of this drug is believed to be against the malaria plasmodia. While there are inadequate data concerning the possible side effects of this drug when administered over a long period of time, there is no evidence that it is habit forming, although obviously a patient who experiences temporary relief from symptoms following its use will come to rely on it at each subsequent attack.

EXHIBITIONISM

To the Editor:—Will you give me some information as to the cause and treatment of exhibitionism. I have a man with this condition and I should like to help him.

M.D., Illinois.

ANSWER:—The problem of exhibitionism is usually related to disorders of the total personality. It is seen in otherwise normal people, in persons with senile psychoses and sometimes in the postepileptic confusional states. Such anomalies of the sexual instinct often give rise to medicolegal problems. It is commonly accepted that there is considerable variation in the intensity of sexual desire in different persons. However, the important factor is not the intensity but the degree of control that can be exerted over such instinctive drive. This control is exercised by mental activity and therefore it is not uncommon to find exhibitionism in subjects who are mentally defective or feeble-minded or suffering from dementia. Furthermore, self control may also be removed in other forms of mental disorder such as states of manic excitement or alcoholic intoxication. Sexual perversions are found in otherwise normal people. The true "pervert" usually finds no pleasure in normal sexual relations and may even be impotent under such conditions. Some of them, however, lead a dual life, may marry and raise a family, at the same time seeking "perverted" satisfaction elsewhere.

In exhibitionism, sexual gratification is sought by the more or less frank exposure of the genitals to members of the opposite sex. This behavior may be impulsive or episodic and is most often carried on by men, usually possessed of superior or average intelligence.

This patient should be given a careful personality study with emphasis on his sexual drive, with an attempt to find the causes for the fixation of his sexual development at this level of satisfaction. Such a person requires prolonged treatment by a psychiatrist with, first, meticulous analysis of the causes and then resynthesis of the personality, so that he may obtain satisfaction on a normal, socially acceptable, adult, heterosexual level.

ENDOMETRIOSIS AND PREGNANCY

To the Editor:—My wife is 28 years of age and has never been pregnant. After considerable pelvic pain of about six weeks' duration her left ovary was removed in November 1939. At operation we found a large chocolate cyst densely adherent to the abdominal wall. The pathologic report is endometriosis with extension into the fallopian tube and abdominal wall. She made a speedy recovery. Her periods have been regular but have been accompanied by increasing pain both in the left flank and in the rectum. Pelvic examination reveals a nodule of increasing size. We wish to have a child before things go wrong. What effect does pregnancy have on endometriosis, especially as to symptoms? What is today the best accepted treatment? Panhysterectomy? Oophorectomy? X-rays? Radium? What about some of the new hormones, such as testosterone propionate, to inactivate the ovary?

M.D., Pennsylvania.

ANSWER:—There is a high incidence of primary and secondary sterility in women who have endometriosis. Among the 131 married patients with endometriosis seen at the Mayo Clinic, 48.9 per cent either had never been pregnant or had had only miscarriages. The absolute sterility rate was 32.1 per cent (Counsellor, V. S.: *Am. J. Obst. & Gynec.* 37:788 [May] 1939). In a series of 238 married women with endometriosis studied by Payne (*ibid.* 39:373 [March] 1940) 40 per cent had never been pregnant. Because of this high incidence of sterility it is generally unwise to preserve the reproductive function in cases in which the disease is diffuse. On the other hand, when the disease is unilateral or when there are only scattered implants on the peritoneum one should always try conservative treatment for women who are desirous of having children and for those under 40 years of age.

At the Mayo Clinic fifty-five women who were capable of having children were treated conservatively but only seven (12 per cent) of them conceived and had ten children. In Payne's series the incidence of pregnancy for conservative treatment was 21 per cent.

Special forms of conservative treatment may be tried. Cooke (*Am. J. Obst. & Gynec.* 37:796 [May] 1939) performed presacral and ovarian neurectomy in four cases of endometriosis and the lesions underwent regression. One of the patients had

two children after the operation. In another case the mass was reduced to a fifth of its original size. Whether the neurectomy had anything to do with the regression is problematic. Pratt (*Am. J. Obst. & Gynec.* 37:796 [May] 1939) believes it is possible to relieve some of the pain due to endometriosis by cutting down the ovarian function. This is done by removing one entire ovary and a half or a third of the other. One patient had three pregnancies following such an operation. The majority of the patients were relieved of pain. Another form of conservative treatment which is at the same time simple is destruction of the areas of endometriosis with the electric cautery.

When pregnancy does occur in a woman with endometriosis it does not produce any special disturbances.

The present patient should make an effort to have a baby as soon as possible. If conception fails to take place and the nodule grows and especially if the pain increases, an operation will have to be done. This is preferable to the use of radium or x-rays because it may be possible to remove the nodule and only the diseased part of the remaining ovary. Likewise it will enable the operator to perform a presacral sympathectomy and ovarian neurectomy to relieve the patient's pain. If radiation therapy is used the entire function of the ovary will most likely be eliminated, resulting in a premature menopause. Of course even if an operation is performed in the present case there is likelihood that in order to produce a lasting cure the entire remaining ovary will have to be removed. However, laparotomy will reveal whether or not this is necessary. If, however, the nodule is in the rectovaginal septum, as it may be in this case, it is wiser to employ radiation therapy because surgical intervention would entail removal of the rectovaginal septum with the risk of a fecal fistula.

In the large majority of cases of endometriosis, operation should be employed because the women are in the reproductive period of their lives. In Payne's series 289 were operated on and only fifteen were irradiated. Complete ovarian ablation was necessary in 48 per cent of the surgical subjects.

Endocrine therapy has thus far been useless in the cure of endometriosis. Testosterone propionate may inhibit ovarian activity but the effect will be only temporary.

HEMATOPORPHYRIN IN MELANCHOLIA

To the Editor:—Recently I have read some articles concerning the use of hematoporphyrin in melancholia of the involutional type. These simply state that a small dose was used both hypodermically and orally. I would appreciate more specific information regarding its use in this state, its dosage and its toxic reactions, if any.

Lawell C. Smith, M.D., Lafayette, Ind.

ANSWER.—There have been several favorable reports on the use of hematoporphyrin for the treatment of melancholia of the involutional type.

Hühnerfeld in 1931 found that injections of hematoporphyrin in animals increased their total motor activity and as a result he used this agent in the treatment of psychotic depressions in thirteen cases.

E. A. Strecker reported its use in the affective psychoses and found that, when hematoporphyrin was administered either orally or intramuscularly or by both techniques to psychotic patients, it seemed to produce activation, in some patients mental stimulation and in others somatic improvement. In fifty-five subjects with affective reactions 36.4 per cent showed sustained improvement, 18.2 per cent moderate clinical improvement, and 18.2 per cent general physical improvement but no change in the course of the psychosis, while 27.2 per cent were not benefited. Moreover, there were no significant changes found in the blood chemistry or general body metabolism of twelve patients carefully studied.

The oral solution commonly used contains 5 mg. of hematoporphyrin hydrochloride per cubic centimeter and in the hypodermic solution there is 2 mg. per cubic centimeter.

Oral administration recommended by Angus consists of ten drops in water three times a day before meals, increasing by one drop each day until a maximum of thirty drops three times a day is given; then decreasing the dose at the same rate until ten drops three times a day is reached, when treatment is discontinued.

Hypodermic administration consists of 0.5 cc. the first day, followed by 1 cc. each for the next eight doses given on alternate days. After a rest of one week the series is repeated, this time starting with 1 cc. followed by nine doses of 2 cc. at two day intervals.

Thorner has reported a case of multiple neuritis following the use of this drug. Slight continuous discoloration is also often related to the hypodermic injection of the drug.

The exact action of hematoporphyrin in melancholia is unknown. Much additional research and more carefully controlled groups of control cases must be studied before any final judgment can be given concerning the effectiveness of this medicament.

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PREVENTION OF SMOTHERING IN INFANTS

To the Editor:—Recently newspapers of this city have recorded several accounts of infants who have apparently smothered to death in their coverings. What would be the most advisable way to cover an infant in order to prevent such a catastrophe? Is there any way of safely fastening the covers to the bed in order to prevent the infant's kicking the covers off during the night and yet not risk strangulation or suffocation? Sleeping bags for infants with a collar-like arrangement around the neck are available. Have any fatalities been reported resulting from the use of these? Have they been shown to be less hazardous to the infant than ordinary covers as far as the danger of strangulation is concerned? There seems to be a trend among younger pediatricians to have newborn and young infants sleep on their abdomens. This supposedly lessens the risk of aspirating mucus or regurgitated material. Has the superiority of the prone over the supine position for young infants been definitely demonstrated? Would the danger of suffocation be greater or less in the prone position? I have noted that infants who sleep in the prone position have a tendency to develop a "froglike" attitude of the extremities and an up-tilted nose. Is there any danger of permanent deformity from the prone position?

M.D., Pennsylvania.

ANSWER.—Undoubtedly many of the newspaper accounts of infants having smothered to death in their coverings are not authentic because when complete necropsies are done on infants who die suddenly in bed it is not uncommon to find other causes of death than suffocation.

However, the following precautions may be taken to prevent such catastrophes: Most important is a firm and hard mattress without sagging, so that the infant cannot slip down in the middle. Infants under 1 month or 6 weeks of age, who cannot raise their heads and shoulders from the bed easily, may be placed on the abdomen or back during the day when some one is in the room watching them; at night it is better to keep them on the side. Especially does this apply to infants during the first weeks, when vomiting is more frequent. The side position may be accomplished by tucking the covers snugly under one side of the infant, the other edge of the covers being tucked firmly under the mattress. Older infants may safely be allowed to sleep on the abdomen. Pillows should not be used.

It is doubtful whether sleeping on the stomach could cause any of the deformities mentioned, but in order to alleviate any possibilities of flattening the head or nose an infant can be placed on its back for twelve hours and on its abdomen for the other twelve hours.

There is less danger of a baby mechanically aspirating regurgitated material when sleeping on its stomach, provided the baby can lift its head and shoulders out of the vomitus.

The safest method of fastening the covers to the bed is to have covers wide enough so that they can be thoroughly and snugly tucked in on the sides under the mattress. The covers should not come any higher or little higher than the nipple line. This and a hard mattress make it practically impossible for the infant to get out of position.

Most of the so-called sleeping bags on the market for infants are safe, provided a hood arrangement does not go over the head and provided the collar fits snugly enough around the neck so that the infant cannot pull its head through the opening down into the bag. These are not advisable, however, for young infants as the neck fit is not small enough as a rule to prevent this. As far as known fatalities have not been reported from the use of the present improved sleeping bags. They are probably no more or less hazardous than wide covers properly tucked in.

Elastic attached to the upper bed posts connected with clips attached to the upper corners of the cover is satisfactory, as the covers are then held fast slightly above the upper level of the infant and cannot become twisted about him.

CHILL WITHOUT FEVER

To the Editor:—A young man was awakened from sleep at 5 a.m. by a severe shaking chill. He still was shaking with a typical chill about twenty minutes later. He had no other complaints and physical examination was negative except for slight redness of the pharynx. The rectal temperature, taken during the chill and one-half hour after the chill, was absolutely normal. About ten minutes after I left the house he suddenly vomited some half-digested "hot dogs" that he had eaten about five hours previously. Later that same morning the patient felt perfectly fine and the temperature was still normal. How can one explain a typical chill without any rise in temperature? Could gastric irritation without nausea or pain preceding the sudden vomitus produce a chill without any succeeding fever?

David E. Zuckerman, M.D., Paterson, N. J.

ANSWER.—One can only speculate as to the nature or the cause of the "typical" chill described. It may be asked What is meant by a typical chill? Presumably the patient felt cold and shivered or had persistent clonic contractions. It would be important to know what the patient's occupation was or what he did on the preceding day and evening. Inhalation of metal fumes, for example, may at times cause delayed reaction with chills, but constitutional symptoms usually develop also. It would be important to know if he had ever had any other convulsive seizures which might have been epileptiform in character. Did the patient sleep in a cold room or become chilled by tossing off his covers? It is common knowledge that chills may follow overexposure to cold, as in swimmers, but they seldom last for twenty minutes. Fleeting chills may follow micturition, supposedly either from the sudden loss of a large volume of warm fluid or from "nervous" causes. It is conceivable that a chill may not be followed by a rise in temperature if the mechanism for the dissipation of heat is intact, but one would then have to assume that perhaps the temperature previously was reduced to subnormal levels and raised to normal by the chill. It is difficult to understand how gastric irritation alone could produce a chill unless it again could be explained on a "nervous" basis. The possibility of indigestion accompanied by a nightmare with an emotional aftermath may also be considered.

SENSITIZING TO MILK BY PARENTERAL INJECTION

To the Editor:—Milk is commonly employed parenterally by intramuscular injections in nonspecific protein shock therapy of chronic pelvic inflammatory disease and other conditions. Is there any danger of sensitizing a patient by injection of milk, thus rendering subsequent injections, say a month or two later, dangerous from an anaphylactic point of view?

Willis P. Baker, M.D., Santa Ana, Calif.

ANSWER.—Sensitization by parenteral injections is in most cases difficult. The type of allergen used is one of the factors which determine the ease and degree of sensitivity that can be induced. For instance, the danger from injections of horse serum is generally known. It has been found difficult, however, to sensitize human beings experimentally with such substances as orris root, egg white and rabbit dander. Nor is there any difference in the susceptibility for atopic and nonatopic individuals becoming artificially sensitive (Simon and Rackemann; Cooke and Vander Veer). Simon and Rackemann found that the degree of sensitivity induced artificially by the injection of rabbit serum was much milder and less permanent than "natural" allergy. However, one should point out the unusual cases of allergy developing in cases in which injections of such substances as liver, and even insulin, have been given. In the former group, especially, severe anaphylactic reactions have been reported.

From this work it appears that an artificially induced sensitivity to milk should be uncommon and not likely to be dangerous. One must, however, point out the danger of giving such injections to patients who are allergic to milk. In these cases injections of milk may be dangerous.

FLUORESCENT LIGHTING WITH ARGON

To the Editor:—I am interested in illumination and desirous of information relative to the new electric gas light put out by Ecolite Corporation, Trenton, N. J.

Andrew L. MacMillan Jr., M.D., Concord, N. H.

ANSWER.—The Ecolite Corporation, along with several others, manufactures a variety of lighting fixtures for the new fluorescent type of bulb in which argon or a similar gas is the electrical conductor. These lamps provide a diffuse, glareless illumination with the production of almost no heat. This type of lamp is frequently referred to as furnishing "cold light." The chief objection that has arisen to these lamps is the stroboscopic effect produced. Although shadows are not prominent, such shadows as may be seen appear to be in motion. This is due to the to and fro surge of the electrical current. This has been overcome by multiple units set at different phases, so that the

stroboscopic effect of one bulb is overcome by the others. The effectiveness of fluorescent bulbs is much influenced by the type of fixture. In the past some fixtures have not been of, praise-worthy design. The fixtures now manufactured and sponsored by a new light manufacturers' association are believed to be free from the undesirable features that may have existed previously.

At the present time fluorescent lighting is chiefly observed in banks, department stores, laboratories, tap rooms, physicians' examination rooms and editorial rooms rather than in industry, auditoriums or homes. However, the field of possible use is large and extension is probable.

THERAPEUTIC USE OF MANURE

To the Editor:—Will you please oblige with the following information:

1. Is or was manure ever used therapeutically in the human body?
2. Is there danger from tetanus and the like?
3. Will the effect of manure be influenced by the addition of (a) phenol, (b) oil, (c) alcohol, (d) mustard, (e) cantharides, (f) capsicum, (g) aconite, (h) petrolatum?
4. Is there a difference between steer manure and cow manure chemically, such as in the content of sex hormones?
5. Can an extract be made of manure?

M.D., California.

ANSWER.—1. Medical writings from the earliest times are replete with references to the use of animal and human excrement as therapeutic agents, both within and on the human body.

2. The danger of tetanus as well as other infective organisms is always present, especially when the manure is used as a poultice. When an extract is made by boiling for some time, the danger is materially lessened.

3. The effect of manure would be influenced by the addition of phenol, oil, alcohol, mustard, cantharides, capsicum, aconite or petrolatum. Naturally, the amount of the agents added would determine the degree of modification of the action. If relatively large amounts were used, the action would be more that of the added medicament.

4. There is no difference chemically (including the content of sex hormone) between the manure of the steer, of the bull and of the cow. Sex hormone is not excreted in the feces. If the urine became mixed with the feces there would be a difference in the content of sex hormone between that of a pregnant cow and that of a bull or steer, but only because of the admixed urine. In some species, small amounts of estrogens are found in the feces.

5. An extract of manure can be made by the usual methods. If alcohol is used as the menstruum, the extract will contain all the alcohol soluble substances. If water is used as the menstruum, the extract will contain the water soluble principles.

CESSATION OF MENSES AFTER ERGOTAMINE TARTRATE

To the Editor:—A married woman aged 32 has attacks of hemierianal headaches accompanied by nervousness and vomiting occurring from fifteen to twenty times a year. Many attacks correspond to the first day of the menses, others do not. During the last year the attacks have been treated with 0.5 cc. of ergotamine tartrate and the patient received prompt dramatic relief when the ergotamine tartrate was given at the onset of the menses. The patient stops flowing within six hours and does not flow again until her normal menstrual period. Is this reaction to ergotamine tartrate harmful to the patient and would you suggest continuation of this method of treatment?

M.D., Washington.

ANSWER.—Presuming that the menstrual history of the patient with headache is within normal limits and presuming that no other changes have occurred from the administration of ergotamine than those stated, it is probably safe to continue treatment as often as twenty times a year without fear of complications.

As is well known, ergotamine is an oxytocic and might be expected to terminate a menstrual period. It is also a vasoconstrictor and would thus decrease hemorrhage. It might be advantageous to try from 10 to 20 mg. of benzedrine sulfate with the ergotamine when given on the first day of the menses. It would be inadvisable to give the ergot to this patient during pregnancy.

SEROUS ATROPHY OF FAT ON EPICARDIUM

To the Editor:—From time to time I have seen marked edema on the surface of the heart at autopsy in advanced cases of pulmonary tuberculosis. Is there any explanation for this edema?

Raymond H. Goodale, M.D., Worcester, Mass.

ANSWER.—The reference is probably to "serous atrophy of fat" which is often observed in the epicardium after severe emaciation. It is essentially an infiltration of the tissue spaces of adipose tissue after bulk has been lost through atrophy of the fat. It is not specific for tuberculosis.

EXAMINATION AND LICENSURE

Medical Examinations and Licensure

JOUR. A. M. A.
JULY 20, 1940

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS
EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, July 13, page 153.

BOARDS OF MEDICAL EXAMINERS

ALASKA: Juneau, Sept. 3. Sec., Dr. W. W. Council, Box 561, Juneau.

ARKANSAS: Regular. Little Rock, Nov. 7-8. Sec., Dr. D. L. Owens, 1415 Main St., Little Rock. Nov. 7. Sec., Dr. Clarence H. Young, Little Rock.

CALIFORNIA: Oral examination (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California). San Francisco, Oct. 2. Written examination. Sacramento, Oct. 21-24. Sec., Dr. Charles B. Pinkham, 1020 N. St., Sacramento.

CONNECTICUT: Endorsement. Hartford, July 23. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden.

DISTRICT OF COLUMBIA: Washington, Nov. 11-12. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Tampa, Nov. 18-19. Sec., Dr. W. M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, Oct. 8-9. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, Oct. 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Oct. 1-3. Superintendent of Registration, Mr. Lucien A. File, Springfield.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, Dec. 3-5. Sec., State Board of Health, Dr. A. T. McCormack, 620 Third St., Louisville.

MARYLAND: Baltimore, Dec. 10-11. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: Lansing, Oct. 9-11. Sec., Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: Minneapolis, Oct. 15-17. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: Helena, Sept. 30. Written. Helena, Oct. 1-2. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: Reciprocity with oral examination. Aug. 5. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW MEXICO: Santa Fe, Oct. 7-8. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Sept. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Building, Albany.

OKLAHOMA: Oklahoma City, Dec. 11. Sec., Dr. James D. Oshorn Jr., Frederick.

PUERTO RICO: San Juan, Sept. 3. Sec., Dr. O. Costa Mandry, Box 3854, Santurce.

TEXAS: Endorsement. Dallas, July 28. Sec., Dr. T. J. Crowe, 918-20 Mercantile Bldg., Dallas.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 4-6. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WISCONSIN: Madison, Jan. 14-17. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, October. Sec., Dr. M. C. Keith, Capitol Building, Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

DISTRICT OF COLUMBIA: Washington, Oct. 21-22. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Gainesville, Nov. 1. Applications must be on file not later than Sept. 16. Sec., Dr. John F. Conn, John B. Stetson University, De Land.

MINNESOTA: Minneapolis, Oct. 1-2. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: Lincoln, Oct. 1-2. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

SOUTH DAKOTA: Examination. Yankton, Dec. 6-7. Endorsement. Dec. 21. Sec., Dr. Gregg M. Evans, Yankton.

WISCONSIN: Madison, Sept. 21. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee.

Rhode Island April Examination

Dr. Robert M. Lord, secretary, Rhode Island State Board of Examiners in Medicine, reports the written examination held at Providence, April 4-5, 1940. The examination covered twelve subjects and included seventy-five questions. An average of 80 per cent was required to pass. Two candidates were examined, both of whom passed. One physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year	Per Cent
Tufts College Medical School	Grad.	(1938)	83.6
Université de Genève Faculté de Médecine	Grad.	(1937)	82.8
School	LICENSED BY ENDORSEMENT	Year	Endorsement
Tufts College Medical School	Grad.	(1938)	N. B. M. Ex.

Alabama Reciprocity Report

Dr. J. N. Baker, secretary, Alabama State Board of Medical Examiners, reports nineteen physicians licensed by reciprocity from January 18 through March 15. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year	Reciprocity with
University of Arkansas School of Medicine	Grad.	(1938)	Arkansas
Emory University School of Medicine	Grad.	(1938)	Georgia
Loyola University School of Medicine	Grad.	(1938)	Illinois
University of Louisville School of Medicine	Grad.	(1938)	Kentucky
Louisiana State University School of Medicine	Grad.	(1936)	Louisiana
Tulane University School of Medicine	Grad.	(1935)	Mississippi
University of Minnesota School of Medicine	Grad.	(1937)	Minnesota
Long Island College of Medicine	Grad.	(1927)	New York
University of Buffalo School of Medicine	Grad.	(1932)	Ohio
Western Reserve University School of Medicine	Grad.	(1938)	Penn.
Temple University School of Medicine	Grad.	(1937)	S. Carolina
Medical College of the State of South Carolina	Grad.	(1933)	Tennessee
University of Tennessee College of Medicine	Grad.	(1938, 3)	Texas
Baylor University College of Medicine	Grad.	(1930)	Virginia
Medical College of Virginia	Grad.	(1919)	

California February Examination

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination held at Los Angeles, Feb. 27-29. The examination covered nine subjects and included ninety questions. An average of 75 per cent was required to pass. Seventy-six candidates were examined, sixty-five of whom passed and eleven failed. The following schools were represented:

School	PASSED	Year	Per Cent
College of Medical Evangelists	Grad.	(1939)	76.4, 77.3, 77.6, 78.1, 78.9, 82.9, 84.6
Stanford University School of Medicine	Grad.	(1939)	76.4, 80.6
University of Colorado School of Medicine	Grad.	(1939)	85.3
George Washington University School of Medicine	Grad.	(1937)	84.8
Northwestern University Medical School	Grad.	(1938)	80.2†
Rush Medical College	Grad.	(1938)	80.2†
University of Illinois College of Medicine	Grad.	(1938)	77.1
The School of Medicine of the Division of Biological Sciences	Grad.	(1927)	82
State University of Iowa College of Medicine	Grad.	(1939)	81.7
Tulane University of Louisiana School of Medicine	Grad.	(1939)	85.3
Johns Hopkins University School of Medicine	Grad.	(1939)	76.1
Boston University School of Medicine	Grad.	(1935)	83.4
Harvard Medical School	Grad.	(1939)	80.2
Wayne University School of Medicine	Grad.	(1939)	80.6
University of Minnesota Medical School	Grad.	(1939)	83.3†
St. Louis University School of Medicine	Grad.	(1939)	87.1
Washington University School of Medicine	Grad.	(1938)	80.9
Creighton University School of Medicine	Grad.	(1939)	76.7
University of Nebraska College of Medicine	Grad.	(1939)	82.6
Eclectic Medical College, Cincinnati	Grad.	(1939)	75.9, 78.9, 79
University of Oklahoma School of Medicine	Grad.	(1935)	82.1
Woman's Medical College of Pennsylvania	Grad.	(1939)	80.6
Baylor University College of Medicine	Grad.	(1939)	76.8, 80.1, 81.9, 86.1
Medical College of Virginia	Grad.	(1939)	78.4, 81.3
University of Virginia Department of Medicine	Grad.	(1936)	84
Marquette University School of Medicine	Grad.	(1936)	76.9
University of Wisconsin Medical School	Grad.	(1938)	77.8
University of Toronto Faculty of Medicine	Grad.	(1939)	79.7
Medizinische Fakultät der Universität Wien	Grad.	(1938)	81.9, 83.7
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	Grad.	(1910)	80.3
Rheinische Friedrich-Wilhelms Universität Medizinische Fakultät, Bonn	Grad.	(1917)	82.8, (1921)
Schlesische Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau	Grad.	(1921)	77.3
Universität Basel Medizinische Fakultät	Grad.	(1925)	85.8
University of Arkansas School of Medicine	Grad.	(1936)	87.6
School	FAILED	Year	Number Failed
College of Medical Evangelists	Grad.	(1938)	1
Rush Medical College	Grad.	(1939)	1
The School of Medicine of the Division of Biological Sciences	Grad.	(1938)	1
Louisiana State University School of Medicine	Grad.	(1936)	1
St. Louis University School of Medicine	Grad.	(1939)	1
University of Oregon Medical School	Grad.	(1939)	1
Hahnemann Med. College and Hospital of Philadelphia	Grad.	(1938)	1
Medizinische Fakultät der Universität Wien	Grad.	(1939)	1
Ludwig-Maximilians-Universität Medizinische Fakultät, München	Grad.	(1937)	1
Latvijas Universitāte Medicīnas Fakultāte	Grad.	(1931)	1
* This applicant has completed four years' medical work and will receive the M.D. degree on completion of internship.		(1923)	1
† This applicant received the M.B. degree and will receive the M.D. degree on completion of internship.			

Book Notices

Diseases of the Gallbladder and Bile Ducts. By Waltman Walters, B.S., M.D., M.S., Head of Section in Division of Surgery, The Mayo Clinic, Rochester, Minnesota, and Albert M. Snell, B.S., M.D., M.S., Head of Section in Division of Medicine, The Mayo Clinic. Cloth. Price, \$10. Pp. 645, with 342 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

Though the names of Walters and Snell on the title page lead the reader to expect a book under their joint authorship and therefore with a large personal element, a scrutiny shows that there are no less than eight additional collaborators in the production of this work. Fortunately, all are members of the staff of the Mayo Clinic, so that the book is a reflection of the activities of that organization in this particular field. It took the reviewer some time to discover that the book was divided into five separate parts, each of which contains from five to nine chapters. This arrangement proves troublesome for, half way through the book, the reader may find himself perusing, say, chapter III, but without any clear indication of the part to which it belongs. Actually there are five chapters III's, at pages 41, 118, 229, 397 and 540, and it is necessary to turn back to the table of contents to discover their appropriate sections. The way the reader is constantly referred from one part of the text to another also is very troublesome. These two blemishes detract from the pleasure one expects from the perusal of such a book, and let us hope that in some future edition they may be corrected. Nonetheless, the work is a storehouse of valuable information representing an enormous amount of labor in its preparation, but it is neither a continuous narrative nor a consecutive surgical story. It ranks more with a first class book of reference than the authoritative work which its size and setup would suggest, to say nothing of the distinction in surgery of its senior author. The book has no less than 645 pages, including the indexes, with 342 illustrations, some of them very good, such as the beautiful colored frontispiece. There are also a great many excellent diagrammatic figures. It is printed on heavy leaded paper, which doubtless enables the illustrations to be brought out clearly but results in the production of a volume weighing three and a half pounds, so that it is not comfortable to handle or read other than at a desk. The foreword by the late W. J. Mayo has rather a sad significance, for it must have been among the last of those numerous communications which we welcomed from his pen. In it he stresses the interest of the historical approach and pays a tribute to pioneers both in Great Britain and in the United States and concludes by propounding some general problems which he thought might perhaps be answered by the study of the pathology of the biliary tract. The sections of the main work on anatomy and physiology contain much useful information, but with all the pictures that are available one misses some of the more ordinary diagrams which are so helpful, especially when anomalies of the ducts are under discussion. Some old favorites like Hartmann and his pouch are not mentioned. From the physiologic point of view the authors do not allow the gallbladder a place of great importance and there is no suggestion, for instance, that its wall may perhaps secrete a hormone of value. It is interesting to be reminded of the rhythmic contractions of that viscus, which might indeed by analogy be expected. The discussion on cholecystitis sets out some interesting points of view. One gathers that the authors are generally in favor of the infective origin of gallstones, but much experimental work and clinical experience will have to be thrown entirely aside if we are to give up the possibility of the influence of some metabolic and chemical factor as causal agents. No stress is laid on the possibility of a calculous diathesis. Under the heading of the pathology of gallbladder disease the remarkable resources of the Mayo Clinic have been fully utilized, and it is indeed striking to read that between 1893 and 1937 nearly 30,000 removed gallbladders were examined in its laboratories. To those of us who have suffered disappointments in the management of cases recognized as of the strawberry gallbladder type it is rather comforting to read that this probably presents only "a phase in the normal excretion of cholesterol and is a part of the mechanism concerned with maintaining the cholesterol constant in the circulating blood."

From the consideration of this large amount of material it is interesting to find that there were only 103 gallbladders which showed evidence of malignant disease. The authors properly point out that the mortality of the removal of stones, though small, is nonetheless greater than the frequency of malignant disease following their presence. But after a review of so much material at close hand it is refreshing to be told that we can hope to get enlightenment on the main problems connected with the diseases of the biliary tract only if they are considered not alone but in connection with the disturbances of the body generally as well as possible associated lesions in the stomach, duodenum, pancreas, liver and large bowel. When the authors come to deal with diagnostic methods it is again comforting to find them insisting on the importance of the history and of ordinary methods of examination. They are conservative about the possible value of the duodenal tube but it would have been interesting to find more detailed information about the actual results of this method of investigation in the authors' own hands in the small group of cases in which it is probably the most important of the few methods of physical examination available.

After the general review of diagnostic methods we pass on to the consideration of the subject of cholecystography with the information that 95 per cent of diagnoses based on this method, whether the signs found are positive or negative, are correct. Nonetheless we are later reminded that the method is not to be looked on as a substitute for clinical examination or to supplant clinical judgment. When the authors write of intervention for noncalculous cholecystitis they emphasize that from clinical experience the result from the patient's point of view depends on whether or not intervention is for the relief of pain. They have found that when the symptoms have a more or less problematic connection with mild changes in the gallbladder the prospects of relief from surgical intervention are indeed small. In this as in other sections it would have been useful to have more of the personal experience of the authors rather than the views of the wealth of authorities which have been consulted and which are referred to in every portion of the book. In discussing cholangitis the authors are delightfully frank, a frankness which will be appreciated by those who have had experience of these cases, for they admit that it is extremely difficult to forecast the full extent of the disease and that secondary abscesses are often only the disclosure of the postmortem room. In treatment one is a little surprised that more stress is not laid on the importance of controlled biliary drainage with an open air and general anti-infection regimen. In the management of benign strictures of the bile duct few surgeons can have had so extensive an experience as Walters, and that makes the section on this particular subject of especial value, and one admires the restraint which the authors follow in talking about the results of surgical intervention in what is admittedly this serious complication. The descriptions of the operative procedures supported by excellent illustrations are good, although the difficulties might with advantage have been more emphasized.

The plan of making a temporary biliary fistula which can later be transplanted into the intestine is mentioned as a way out in difficult cases and is certainly safer than an endeavor to make an anastomosis or a reconstruction at all costs. The authors confess that in spite of an immediate mortality of 12.5 per cent relief of the obstruction and control of the infection can be looked for in only about 55 per cent of the cases. That is a state of affairs which cannot be overemphasized as an illustration of the extreme importance of the operation of cholecystectomy and the necessity for attention to every little detail that may render this terrible accident less frequent.

The chapter on the differential diagnosis of jaundice illuminates the well known difficulties of that subject and the fact that the authors stress the importance of its medical management again shows that they keep an open mind, probably engendered by their large experience of surgery in many unpromising conditions. In describing operations the authors are at their best, and what they say is obviously based on an extensive experience. When dealing with cholecystectomy it would have been better to emphasize in the illustrations the extreme importance of the visualization of the three ducts before what is supposed to be the cystic duct is caught or tied. This point is mentioned in the text, though it is not sufficiently stressed. The method of electrocoagulation is assigned its

proper place as one of the methods which may be used where partial cystectomy is called for. It is an operation which undoubtedly fulfils a place but with the remarkably low mortality which the authors can place before the profession there is nothing to justify its employment as a frequent substitute for the more formal operation of cholecystectomy. In the surgery of the common duct the T tube is warmly advocated, but nothing is said about the possible damage to the duct which may be inflicted during its removal. For stones that cannot be removed or that have been "left over" as demonstrated by cholangiography, Pribram's ether dissolving method is commended, but the method is likely to be infrequently called for and is regarded in its proper perspective. The review which the authors gave of the large numbers of operations on the biliary tract which were carried out in the Mayo Clinic during the years 1937-1938 is illuminating; the record is something to be proud of and furnishes standards to attain which others ought certainly to strive. In the operation of cholecystogastrostomy an opening 2 cm. in diameter is suggested, but it would have been well to point out that in these circumstances the anastomosis often contracts and that a much bigger opening, certainly one that freely admits the thumb, is probably none too large. The mournful outlook in intervention for malignant diseases of the pancreas with a mortality of more than 28 per cent cannot be looked on as surprising. W. J. Mayo used always to say that in doubtful conditions about the head of the pancreas an anastomosis was well worth while because there was always the chance that after all the diagnosis of cancer might be wrong, and that is an attitude which should be remembered by those responsible for dealing with these cases.

The chapter on the care of patients before and after operation is full and complete. The authors point out that the condition of the liver is really the key to the situation. Those who have taken most interest in this question will cordially agree with the statement that "to evaluate the general condition of the patient is not difficult, but to attempt to measure accurately the degree of hepatic function is still a baffling problem."

In the consideration of the after-results of cholecystectomy Howard Gray, one of the collaborators, states emphatically that erroneous diagnosis is probably one of the most important factors in the persistence of symptoms following the removal of the gallbladder and writes "The existence of postcholecystectomy syndromes emphasizes the necessity for conservatism in the performance of cholecystectomy."

This book, with its large number of references, is an encyclopedic guide to the literature of the subject, but its really valuable appeal is made when the personal experience of the authors is recounted, backed by the truly remarkable collective resources of the Mayo Clinic to which they owe allegiance.

Morphologische Veränderungen im Knochenmark und Blut bei akuten Blutungsanämien. Von Jarl Forssell. Acta medica Scandinavica, Supplementum CL Paper. Pp. 239, with 38 illustrations. Helsingfors: Mercator Tryckeri, 1939.

This monograph is devoted to the study of the morphologic changes of the peripheral blood and bone marrow following acute hemorrhage in man. The bone marrow was aspirated at the sternum according to the method of Arinkin and from 0.1 to 0.2 cc. was aspirated. Differential counts were made from a study of 1,200 cells in each case. Peripheral blood studies were made during fasting, and blood from the finger was used. Complete studies were made, which included Price-Jones curves, cell volume and reticulocyte counts as well as the routine tests. Eighty-three cases were studied, subdivided into four groups: normal cases of twenty, sexes equal; eight normal women pregnant from two to eight months; fifty cases of acute hemorrhage following abortion from two to five months; cases of acute posthemorrhagic anemia due to gastric and duodenal ulcer, hemorrhoids and epistaxis. A brief summary of all the cases is given. The author presents numerous protocols of the blood examinations. The peripheral blood and bone marrow values agree with those recorded in medical literature. The eight normal pregnant women show peripheral blood values within normal limits except for a slight elevation of leukocytes and a moderate left shift of myeloid cells without neutrophilia. The results of the bone marrow study indicated that pregnancy did not produce a specific bone marrow pattern.

The data from patients with acute hemorrhage are presented in tabular form and are discussed in detail. Liver therapy, arsenic and iron therapy in acute posthemorrhagic anemia are next considered. The author observed that in no case did the liver therapy produce an erythroblastic hyperplasia which was equal to that observed with iron and arsenic. The effect of arsenic on the bone marrow was difficult to explain. The results of the author's observations are summarized at the end of the monograph. The work represents a great deal of painstaking work and careful analysis. There are eight pages devoted to pertinent bibliographic references, fourteen pages containing thirty graphs, and four plates showing eight illustrations of bone marrow cells. The text includes forty-four tables and five diagrams. The monograph is of particular interest to the hematologist, who should derive much factual data from this comprehensive study.

On Oxidation, Fermentation, Vitamins, Health and Disease. By Albert v. Szent-Györgyi, M.D., Ph.D., D.H.C., Professor of Medical and Organic Chemistry, University of Szeged, Hungary. The Abraham Flexner Lectures Series Number Six. Published for Vanderbilt University. Cloth. Price, \$2. Pp. 109, with 14 illustrations. Baltimore: Williams & Wilkins Company, 1939.

The volume contains the five lectures comprising the sixth series of Abraham Flexner lectures delivered by Dr. Albert v. Szent-Györgyi in 1939. They represent a summary of Dr. Szent-Györgyi's experiments in the field of biologic oxidation. The book covers the field of oxidation and includes vegetable oxidation. Its climax is the fifth chapter, or lecture, on vitamins, health and disease. The second and third lectures deal with the respiration of muscles and with fermentation, thus giving a smooth transition to vegetable oxidation. The author presents chiefly his own researches, but he brings them into proper perspective as parts of a broad review of the biochemical basis of life. It may be stated that Dr. Szent-Györgyi elevated himself with these lectures to one of the "praeceptores mundi." The brilliance of his style, the clear and fascinating presentation of the subject, makes the reading of this small volume an exceptional delight. The author leads along the fields of biologic oxidation with an ease which enables one to understand the subject even without a particular knowledge of biochemistry.

The Toothbrush: Its Use and Abuse. A Treatise on Preventive Dentistry and Periodontia as Related to Dental Hygiene. By Isador Hirschfeld, D.D.S., F.A.A.P., Associate Professor of Dentistry, Department of Periodontia, School of Dental and Oral Surgery, Columbia University, New York. Cloth. Price, \$7.50. Pp. 591, with 415 illustrations. Brooklyn, New York: Dental Items of Interest Publishing Company, Incorporated; London: Henry Kimpton, 1939.

This textbook, as the name implies, is developed about the toothbrush and the important part it plays in preventive dentistry and the maintenance of oral cleanliness. The first chapter deals with the evolution of the toothbrush starting from before the Christian era and leading up to present times. This includes many illustrations of ancient articles, both brush type and pick type, which were used in attempting to maintain mouth hygiene. Obviously little advancement has been made in the last hundred years as far as toothbrush design is concerned. Formulas of early dentifrices are also given in this chapter.

The next portion of the book is divided into two main parts: the effects, beneficial and harmful, of the toothbrush on the soft tissue and the effects of the toothbrush on tooth structure itself. The first part includes such conditions as suppurative periodontoclasia, chronic marginal gingivitis and chronic hypertrophic gingivitis, along with many types of traumatizations due to improper handling of the brush and the use of certain dentifrices and mouth washes. The second part includes dental caries in its relation to the toothbrush and abnormalities found on the teeth which may be aggravated by or are definitely caused by the brush. All the conditions referred to in the text are well illustrated, showing cases before and after treatment in which the use of the toothbrush was an important factor. Dr. Hirschfeld points out in this section the importance of determining the cause of abnormalities in the mouth and the methods by which these determinations can be made. This portion of the book is interesting and beneficial to the dental practitioner as it covers almost every type of mouth abnormality which might be aided or abetted by the use of the toothbrush. The chapters on dental caries and food impactions are also well

written and illustrated, showing proper methods of prevention of both, using restorative measures and the toothbrush.

The remainder of the book deals with methods of tooth brushing, along with types of dentifrices and mouth washes, both beneficial and harmful. These few chapters would be helpful to the layman as they are simply written; the fact that they deal also with commercial mouth washes and stain removers, many of which are harmful, would make them interesting reading for almost any one.

Although many conditions are discussed which have no definite bearing on the brush, they are nevertheless all important factors which come under the heading of mouth hygiene and preventive dentistry. The easy reading and good illustrations of everyday oral disease make the book a valuable reference book for dental students and dentists.

Exercise and Keep Fit. By Terry Hunt. Foreword by Ernst Lublisch. Cloth. Price, \$1.96. Pp. 202, with illustrations. New York: Prentice-Hall, Inc., 1940.

The author of this book is said to be "Hollywood's ace conditioner of movie stars and business executives," and his breezily written pages are the lineal descendants of a long line of ancestors written by trainers who have been successful in the handling of newsworthy Americans. He does not pretend to medical knowledge and yet most of what he has written in this volume would be accepted as sound advice by those who have such knowledge. Some of it would not. For example, he advises the reader to "increase resistance to illness by deep breathing in fresh air" and to "take a hot soap bath at least once a week before retiring" and to "give your body a good rubbing with ordinary table salt once a week." There would be considerable doubt among the medical men as to the efficacy of the first, many persons would be kept awake by a really hot bath before retiring, and probably a rub with a rough towel would be quite as helpful as one with salt. The first part of the book gives advice on muscular development, diet, the emotions, sleep, cathartics, care of the skin, the feet and posture—the kind of thing which has been printed in the innumerable books on personal hygiene. And the advice is good! The last part gives illustrated calisthenic exercises, many of the pictures being posed by cinema stars or successful business or professional men. The exercises are not new nor are they any better or worse than those which have appeared in many earlier books of the sort. The final chapter concerns itself with a list of the names and some of the characteristics of the great and near-great persons trained by the author. Possibly the implication is that one who takes the prescribed exercises will be great or near-great. On the whole it is a readable presentation of material, good in the main, which has been printed in a much more scientific, complete and dependable form in many other volumes, such as those by Dr. Jesse Williams.

Fundamentals of Biochemistry in Relation to Human Physiology. By T. R. Parsons, B.Sc., M.A. Sixth edition. Cloth. Price, \$3. Pp. 461, with 26 illustrations. Baltimore: William Wood & Company, 1939.

"When we possess . . . the knowledge . . . of the architecture of the living matter . . . we may be able to give a rational explanation of the circumstance that the world of difference between maleness and femaleness depends on the presence or absence of nothing more romantic than an extra hydroxyl or methyl group, or a double bond more or less, associated with the same all pervading sterol skeleton." With this dream of a great scholar ends the new chapter added to the sixth edition of the book. The other chapters too gained lesser emendations at points where the earlier account needed revision, and according to these revisions the bibliography of various chapters has been improved, some obsolete books having been omitted and newer publications substituted. The new chapter has grown out of a brief supplement of the chapter (VIII) about fats and their metabolism. This supplement said only a few words about the structure of cholesterol and some derivations of the sterol skeleton, the ergosterone, androsterone and estrone. The new chapter (IX) gives a brief report about sterols and steroids. After having demonstrated the essential skeleton of the molecule of cholesterol, i. e. the skeleton of all sterols, the author shows the derivation from the same root of ergosterol, estrone, progesterone, androsterone and corticosterone. He emphasizes the fact that in case of some sterols, as estrone and

androsterone, the corresponding secondary alcohol is several times as potent as the ketone itself. The book in its improved and somewhat augmented form is a true guide, as it was in its earlier publications, in the field of biochemistry.

Minor Surgery. By R. J. McNeill Love, M.S., F.R.C.S., Surgeon, Royal Northern and Metropolitan Hospitals, London. Cloth. Price, 12s. 6d. Pp. 369, with 155 illustrations. London: H. K. Lewis & Co., Ltd., 1940.

This is a pocket size but excellent work on the subject. However, as the author himself indicates, it is a rather difficult task to determine what is "minor" and what is "major" in surgery. It seems that a discussion of history taking as it pertains to duodenal ulcer or cholelithiasis is completely out of place in a work called "Minor Surgery." The same applies to examination for acute abdominal conditions, preparation of the patient for operation, and the technic of cystoscopy or operation for hydrocele. Yet when one considers that the purpose of this volume is to be a guide to hospital residents called on to deal with common emergencies or minor surgical problems, it is understandable and forgivable. The title, however, may be changed to "Surgical Manual for Hospital Residents." The book is written unusually well, in clear concise language. The material is entirely abreast of the time from both the diagnostic and the technical point of view. A great deal of subject matter is included between the covers of this small volume. The illustrations are adequate and illuminating. The book is highly recommended for the purpose intended.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Administration of Atropine for Plastic Iritis or Glaucoma; Alleged Abandonment of Patient.—About April 1, 1934, Saunders, a man slightly over 50, consulted the defendant physician, an eye, ear, nose and throat specialist, relative to an ailment of his left eye. The physician diagnosed the plaintiff's ailment as plastic iritis and instituted a course of treatments with atropine. The patient visited the physician's office two or three times a week for observation and treatment. On May 22 or 23, after examining the patient's right eye on request, the defendant administered "some treatment to the right eye, and from then on it never cleared, and excruciating pain and agony was felt by the plaintiff." Thereafter the physician treated both eyes. In June the patient lost his vision in both eyes, which loss apparently was permanent. Some time in October he became unable physically to continue his visits to the defendant's office. According to the patient, during October and November, by telephone, he repeatedly urged the defendant to call on him at his home, but the defendant refused to do so. A general practitioner, Dr. Bryans, informed the defendant that he had visited the patient after the defendant's refusal and had found him nauseated, weak and suffering from severe pains in his head. On December 1, Dr. McLane, an eye specialist, was called. He found the patient suffering from glaucoma, a condition characterized by a hardening of the eyeball. Subsequently the patient sued the defendant physician for malpractice, alleging, in effect, that the bad result was due to the unskilful and negligent manner in which the defendant had attended and treated him. The trial court directed a verdict for the physician and the patient appealed to the Supreme Court of Florida, Division B.

At the trial there was uncontradicted medical testimony that (1) the administration of atropine is the recognized standard treatment for plastic iritis, but that if such drug is administered the physician must see and observe the patient every forty-eight to seventy-two hours in order to check or test the intraocular "tension" or pressure; (2) if a patient appears to be hypersensitive to atropine, or any other drug, due care requires that a close check be kept and the drug changed so as not to cause the patient pain or agony; (3) a glaucomatous eye first appears red and later white, and the eyeball, while its shape may or may not be changed, has a tendency to appear to be pushed outward; (4) glaucoma in its early stages may be reme-

died by drugs or surgery; (5) plastic iritis, an involvement of the iris with adhesions, frequently develops into glaucoma, and (6) in the locality in question it is customary for a physician to visit his patient when the latter is physically unable to come to the physician's office.

It is not clear from the published report whether or not the facts just stated were sufficient to require the trial court to permit the jury to pass on the question of the alleged negligence of the defendant physician. Relying chiefly on 48 Corpus Juris, par. 113, pp. 1125, 1126; par. 115, pp. 1128, 1129 and par. 116, p. 1129, the Supreme Court discussed the general rules of law relating to (1) the burden which rests on the plaintiff in a malpractice suit to show that the defendant was unskilled or negligent and that his unskilfulness or negligence resulted in harm to the plaintiff, (2) the liability of a physician for an erroneous diagnosis and (3) the duty of a physician, in the absence of an agreement to the contrary, to continue in attendance until dismissed by the patient, or until his services are no longer required, or until he has properly withdrawn from the case after giving the patient reasonable notice. Referring to the defendant's contention that during the period of his treatment the patient's ailment was iritis and that there was but little intra-ocular pressure present, the Supreme Court called attention to the trial court's refusal to permit Dr. McLane to answer the following hypothetical question propounded to him:

Doctor, from his condition of the glaucoma and with a hypothesis that in July and September a layman observed the conical shape and pressure of his eye, how long would you say that glaucoma had existed at the time you saw him?

If the trial court had permitted Dr. McLane to answer this question a possible conflict of opinion would have developed which would have required the trial court to submit the matter to the jury. In fact, there already was a dispute as to the appearance of the diseased eye. Likewise, an inference could have been drawn that the pain and agony suffered by the plaintiff was due to the atropine as prescribed, and that if the defendant had contacted his patient at more frequent intervals this condition could have been alleviated. If, concluded the court, the evidence is conflicting or will permit of different reasonable inferences, or if there is evidence tending to prove the issues, it should be submitted to the jury for its determination as a question of fact and not taken from the jury and passed on by the court as a question of law.

Accordingly, the Supreme Court reversed the judgment of the trial court and, in effect, ordered the case retried.—*Samuders v. Lischkoff (Fla.)*, 188 So. 815.

Workmen's Compensation Acts: Death from Torulosis Allegedly Aggravated by Trauma.—In the course of his employment, December 19, the workman was struck on the head by a ladder and sustained a scalp wound. He was taken immediately to a physician who treated his wound. He returned for further treatments on December 21 and 24. He continued his usual employment until January 19, although his capacity for work was perceptibly impaired. He complained of pain in his head, his condition became progressively worse and he was "very weak and very thin" and could not walk without staggering from side to side. He was admitted to a hospital January 31 where he died February 28. A referee awarded his widow compensation under the Minnesota workmen's compensation act, and the employer and his insurer appealed to the industrial commission of Minnesota.

An autopsy was performed at which were present all the medical expert witnesses who subsequently testified at the hearing before the commission. Sections were removed from the brain and spinal cord for microscopic examination. It was concluded that death resulted from torulosis (an infection with *Torula*, a fungus), involving the central nervous system, and that the disease was present prior to the time of the injury. At the hearing a pathologist, called by the employer and his insurer, emphatically insisted that the workman died as a result of torulosis and that the accident in no way contributed to his death. Three physicians, on the other hand, testifying for the widow, agreed that the industrial accident aggravated the pre-existing condition of torulosis to such a degree that death was attributable thereto. It was agreed by all these medical wit-

nesses that torulosis is such an extremely rare disease that less than sixty cases had been recorded in medical history and their actual experience with respect to this condition was limited to this particular instance. A "neutral pathologist," appointed by the commission, after reviewing the entire record of testimony and microscopically studying the sections taken from the workman's brain and spinal cord, testified that the primary cause of death was torulosis and added:

The fact that the development and advance of the disease is dependent upon the immunity of the individual; because there is reasonable evidence to show that there was trauma to the brain; because trauma can produce situations similar to those which favor the growth of the organisms, and thus disturb the balance against any prior resistance; and because of the sudden appearance of symptoms following the trauma in an individual supposedly previously well, it is my opinion that there exists a reasonable probability that the injury aggravated the disease.

The commission then awarded compensation to the widow, and the employer and his insurer appealed to the Supreme Court of Minnesota.

The appellants contended that the record did not sustain a finding of causal connection between the industrial injury received and the workman's death. They argued that since the pathologist who testified in their behalf was "exceptionally qualified" his opinion was entitled to more weight than that of the medical witnesses called by the widow, who did not claim to be "expert pathologists." The fact, said the Supreme Court, that the pathologist called by the appellants was "exceptionally qualified" does not permit this court to cast aside the opinion of the other expert witnesses. It was for the commission, the triers of fact, to determine what must be, in its very nature, a fact issue. It was the opinion of the court that as a court of review it was necessarily limited to a determination of whether there was sufficient evidence to sustain the result reached by the commission.

It may be conceded, continued the court, that the workman's disease was present in his body at and prior to the time of the accident but that was not conclusive against a finding of liability, since the application of the workmen's compensation act is not restricted only to those who are normal or strong in body. The act does not exclude the weak or physically unfortunate. Latent and unknown tendencies to disease are common and the legislature in passing this law must have had in mind the fact that such latent ailments or maladies may develop into serious conditions if incited to activity by what might otherwise be regarded as trivial accidental injuries in the course of employment. If the workman's infirmity or disease was in fact accelerated by the injuries to his head, as the commission found, his widow was entitled to recover compensation, not on the theory that the injuries caused the disease that already existed but because of the effect of such injuries on that disease. The court held that it was bound by the commission's finding because, while this might be a "borderline" case, it did not believe that the opinions of the physicians who testified for the widow were so inconsistent with reason and common sense as to justify it in rejecting them. Accordingly the award of compensation in favor of the widow was affirmed.—*Westereng v. City of Morris (Minn.)*, 285 N. W. 717.

Society Proceedings

COMING MEETINGS

- American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.
- Colorado State Medical Society, Glenwood Springs, Sept. 11-14. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.
- Idaho State Medical Association, Sun Valley, Sept. 11-14. Dr. J. N. Davis, 204 Fourth Ave., East, Twin Falls, Secretary.
- National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
- Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
- Virginia Medical Society of, White Sulphur Springs, W. Va., July 29-31. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.
- Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
- West Virginia State Medical Association, White Sulphur Springs, July 29-31. Mr. Joe W. Savage, Public Library Bldg., Charleston, Executive Secretary.
- Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

19:513-638 (May) 1940

- *Production of Pressor Substance by Totally Ischemic Kidney. A. C. Taquini, Buenos Aires, Argentina.—p. 513.
Two Unusual Types of Electrocardiograms. H. B. Weinberg and L. N. Katz, Chicago.—p. 519.
Immediate Effects of Intravenous Administration of Neoarsphenamine on Electrocardiogram in Cases of Syphilitic Aortitis. C. L. Tung and J. W. Mu, Peiping, China.—p. 529.
Responses of Blood Vessels in Resting Hand and Forearm to Various Stimuli. D. I. Abramson and E. B. Ferris Jr., Cincinnati.—p. 541.
Effect of Certain Drugs on Coronary Blood Flow of Trained Dog. H. E. Essex, R. G. E. Wegria, J. F. Herrick and F. C. Mann, Rochester, Minn.—p. 554.
Studies on Mercurial Diuresis. III. Alteration Induced in Cerebrospinal Fluid Pressure. I. F. Volini and R. O. Levitt, Chicago.—p. 566.
Study of Precordial Leads in Subjects with Congenital Dextrocardia and Situs Inversus Viscerum. A. T. Ogaard, N. W. Voorhies, G. E. Burch and S. C. Cordill, New Orleans.—p. 571.
Clinical Comparison of Crystalline Glucosides of Digitalis Lanata (Digilanid) and Powdered Leaf of Digitalis. W. Adams and L. Gregg, Chicago.—p. 576.
Bacterial Endocarditis Superimposed on Syphilitic Aortic Valvulitis: Review of Literature and Presentation of Five Cases. J. Wright and Pearl M. Zeck, Cincinnati.—p. 587.

Production of Pressor Substance by Ischemic Kidney.

—Taquini performed experiments on dogs to learn whether the totally ischemic kidney can produce arterial hypertension, whether it produces a pressor substance and, if there is such a substance, the mechanism of its action. He produced total renal ischemia in ten dogs. In five in which renal circulation was reestablished, after from five and one half to six and one half hours of total ischemia an increase in arterial pressure resulted. In five dogs whose renal circulation was not reestablished the arterial pressure remained unchanged. He grafted sixteen totally ischemic kidneys into the necks of sixteen normal dogs to learn how the hypertension is produced. He found that in ten experiments, when the ischemia was complete, there was a definite rise of blood pressure in nine of the recipient dogs; in the other six experiments, in which the ischemia was not complete, in four because of the remaining collateral circulation and in two because only one of the two renal arteries supplying each kidney was occluded, grafting produced no change in blood pressure. The fact that the totally ischemic kidney liberates a pressor substance into the blood has been confirmed by direct injection of blood from the renal vein. One kidney pedicle of the dog was clamped for six hours, after which blood was collected from this and from the other kidney vein. Blood (100 cc.) from the clamped kidney was injected and a definite rise was observed, whereas normal blood produced no change in blood pressure. It appears that acute, complete ischemia of the kidney produces a pressor substance, as does the partially ischemic kidney. The substance liberated by kidneys which have been rendered acutely and totally ischemic acts like that produced by the partially ischemic kidney directly on the peripheral vascular system causing vasoconstriction and hypertension.

American Journal of Clinical Pathology, Baltimore

10:319-360 (May) 1940

- Placental Infarction and Edemapsia. H. F. Hunt, W. B. Patterson and R. E. Nicodemus, Danville, Pa.—p. 319.
Icteric Meso-Aortitis with Aneurysm of Thoracic and Abdominal Aorta: Case Report. A. Levitt and D. S. Levy, Buffalo.—p. 332.
Cryochem-Preserved Complement of Guinea Pig Serum. E. W. Florsdorf, F. Boerner, M. Lukens and T. S. Ambler, Philadelphia.—p. 339.
Symptomatic Renal Fibrosarcoma with Spinal Metastases: Report of Case. W. L. McNamara, H. D. Smith and W. A. Gore, Los Angeles.—p. 345.

American Journal of Medical Sciences, Philadelphia

199:601-748 (May) 1940. Partial Index

- *Studies on "Essential" Hypertension: III. Effect of Nephrectomy on Hypertension Associated with Organic Renal Disease. H. A. Schroeder and G. W. Fish, New York.—p. 601.
Role of Kidney in Pathogenesis of Arterial Hypertension. E. Dicker, Brussels, Belgium.—p. 616.
Essential Hypertension: Comparison of Hypertensive and Nonhypertensive Phases Following Coronary Thrombosis. H. Gross and H. Engelberg, New York.—p. 621.
*Painless Myocardial Infarction. H. M. Pollard and T. H. Harvill, Ann Arbor, Mich.—p. 628.
*Etiology of Idiopathic Pneumothorax. H. J. Lorge, Rutland, Mass.—p. 635.
Negative Results of Irradiation Therapy of Pylorus and Brunner's Gland Area in Patients with Polycythemia Vera. K. W. Stenstrom, P. H. Hallock and C. J. Watson, Minneapolis.—p. 646.
Use of Intravenous Sodium Chloride in Pyrotherapy. E. E. Rosenberg and N. N. Epstein, San Francisco.—p. 650.
Rotenone in Treatment of Scabies: New, Nonodororous, Nonirritating Form of Treatment—Preliminary Report. Carmen C. Thomas, Philadelphia, and Evelyn E. Miller, Vineland, N. J.—p. 670.
Absorption of Sulfanilamide as Index of Blood Flow in Intestine of Man. E. A. Stead Jr. and P. Kunkel, Boston.—p. 680.
Vitamin A Status of Families in Widely Different Economic Levels. Pauline Beery Mack and Agnes Pauline Sanders, State College, Pa.—p. 686.
Relationship of Dietary Intake of Nicotinic Acid to Coenzyme I Content of Blood. A. E. Axelrod, E. S. Gordon and C. A. Elvehjem, Madison, Wis.—p. 697.
Influence of Season on Severity of Diabetes and Its Sclerotic Complications. L. B. Owens and C. A. Mills, Cincinnati.—p. 705.
Effects of Cigaret Smoking and Deep Breathing on Peripheral Vascular System: Studied by Five Methods. M. G. Mulinos and I. Shulman, New York.—p. 708.

"Essential" Hypertension and Organic Renal Disease.

—From their observations on seven patients, Schroeder and Fish conclude that removal of a diseased kidney does not consistently alter the course of arterial hypertension in a favorable direction. Only two patients were definitely improved. These results indicate that the injured kidney was not the sole source of hypertension and that other factors may occasionally be of some importance. However, removal of a kidney was followed by a lower blood pressure level of all patients for weeks or months. It is difficult to believe that any major surgical procedure would have produced this result, as in some the improvement was prolonged, but in one instance a further operation, partial gastrectomy, caused a rise in blood pressure. Some change in the pathologic physiology of the circulation occurs after nephrectomy, which the authors believe is due to the removal of at least one factor causing hypertension. All kidneys removed from these patients showed in addition to inflammatory and noninflammatory lesions varying degrees of arterial and arteriolar sclerosis. The least degree of vascular disease was found in the two patients with the best results. However it is not certain that the degree of vascular disease in one kidney is the same as that in the other. There was a marked difference in one case. With the exception of one case, favorable results appeared proportional to the amount of disease of the renal arteries. Further evidence that renal lesions are not the sole cause of arterial hypertension is their presence when the arterial pressure is not elevated. Continuance of an elevated blood pressure after the affected kidney is removed may be explained by the part vascular or other disease in the remaining kidney plays. The authors suggest the following criteria for selection of essential hypertensive cases suitable for therapeutic nephrectomy: 1. It should be known that the arterial hypertension is recent. The time is arbitrarily set at two years. 2. The renal lesion should be confined to one kidney, decreasing its function. 3. Renal function should be within normal limits. 4. Retinitis should be absent and changes in the caliber of the retinal vessels should be minimal. 5. Arterial pressure should be persistently elevated. Unless suitable cases are selected, many kidneys may be removed needlessly without benefit. Patients with long standing hypertension with a so-called malignant course are not good subjects for this form of therapy.

Painless Myocardial Infarction.—Pollard and Harvill determined the frequency of painless coronary occlusion in 375 cases of coronary occlusion. The determination was based on clinical features, electrocardiographic observations and available necropsy material. There were seventeen instances (4.5 per cent) of undoubted coronary occlusion in which no pain, sub-sternal pressure or other "anginal" symptoms had occurred at

any time. In another fifteen cases (4 per cent) there had been no pain or anginal symptoms, but myocardial infarction was strongly suspected even though the electrocardiographic signs were not pathognomonic. Among the symptoms which occurred at the time of the accident in the seventeen undoubted cases, the most common were dyspnea, nausea and vomiting, dizziness and fainting or collapse.

Etiology of Idiopathic Pneumothorax.—Lorge cites nine cases of idiopathic pneumothorax which support Kirshner's conception that the disease will "occur in young people who rarely show emphysema and spare the aged in whom emphysema is fairly common," that idiopathic pneumothorax may be the result of "a congenital pleural defect or an acquired pleural defect with a congenital anlage" and that the formation of pleural blebs may be a secondary manifestation of a primarily weakened pleura. The cases reported strongly suggest that in the idiopathic form of spontaneous pneumothorax one is dealing with a primary constitutional inferiority of the pleural structure. One or more attacks of spontaneous pneumothorax were precipitated in the nine patients by petty causes or no evident cause. One patient died after hemopneumothorax. The other eight patients were clinically well after the collapsed lung had reexpanded. No tuberculosis or any other lesion could be demonstrated. None of the nine patients were more than 46 years of age, seven were less than 35, four less than 25. This obvious incidence of the disease among the young should exclude pulmonary emphysema as an etiologic factor. Its occurrence in women is considered an exception. The author's nine patients were male. Age and sex incidence thus suggest a constitutional factor. In the majority of cases complete collapse is the rule. This is explained by the absence of adhesions between the parietal and visceral pleural leaves. No adhesions were demonstrable in the eight well patients. In the majority of cases evidence of effusion was absent; this again suggested functional impairment of the pleura. Considering the sluggishness of the pleural response, repeated collapse of the same lung is not surprising. In spontaneous or artificial collapse of the lung the pleural leaves tend to become adherent to one another after reexpansion has taken place. This does not seem to be the case in idiopathic pneumothorax. Idiopathic pneumothorax is thus apt to appear in the form of recurrent pneumothorax. The familial occurrence of idiopathic pneumothorax is in favor of its being a constitutional disease.

American J. Obstetrics and Gynecology, St. Louis

39:733-918 (May) 1940. Partial Index

- Decidua-like Changes in Endometrium Without Pregnancy. R. W. Te Linde, Baltimore, and E. Henriksen, Los Angeles.—p. 733.
Salt Poor Diet and Its Effect on Labor. E. E. Wadlow, St. Joseph, Mo.—p. 749.
*Advanced Abdominal Pregnancy, with Special Reference to Management of Placenta, with Report of Three Cases and Review of Literature. L. W. Mason, Denver.—p. 756.
Effects of Diethyl Stilbene (Stilbestrol) on Menopausal Symptoms. J. Huberman and M. J. Colner, Newark, N. J.—p. 783.
Hematometra and Hematocolpos Following Administration of Stilbestrol. A. W. Diddle and W. C. Keettel, Iowa City.—p. 791.
Treatment of Senile Vulvovaginitis with Estrogenic Ointment. D. R. Mishell, Newark, N. J., and L. Motylloff, New York.—p. 796.
Pregnancy and Heart Disease. N. Flaxman, Chicago.—p. 814.
Vitamin B₁ Deficiency as Etiologic Factor in Pregnancy Toxemias: Part II. A. C. Siddall, Oherlin, Ohio.—p. 818.
Roentgenologic Survey of Chest in Pregnant Women. H. J. Perlberg, Jersey City, N. J.—p. 826.
Cancer and Fibromyomas of Uterus. D. D. Bowers, Indianapolis.—p. 830.
Pregnancies After Nephrectomy for Tuberculosis. E. Lissack, Concordia, Mo.—p. 854.
Technic for Aspirating Viable Spermatozoa from Cavity of Uterus as Further Study in Sperm Behavior: Preliminary Report. A. I. Weisman, New York.—p. 875.
Prenatal Injury of Fetus. H. A. Schwartz, New York.—p. 881.
Anterior Pituitary Test for Early Pregnancy. H. G. Hadley, Washington, D. C.—p. 894.

Management of Placenta in Advanced Abdominal Pregnancy.—Mason reports three cases of advanced abdominal pregnancy and reviews the sixty-six cases reported in the English literature from 1933 to 1939. The condition, while not common, is not as rare as is generally supposed. A correct preoperative diagnosis is made in considerably less than half of the cases. The several constant factors that are of value in the diagnosis of late abdominal pregnancy are: (1) a history of signs and symptoms of early ectopic pregnancy with probable tubal abor-

tion, (2) fetal movements that are unusually noticeable and painful to the mother, (3) the unusual ease with which the fetus can be palpated, (4) malaise and general disability unexplained by the pregnancy itself, (5) the resemblance of the cervix to the nonpregnant cervix, (6) frequently a history of beginning labor which persisted for a time and ceased and (7) the uterus, which is frequently palpable. The presence of any one of these factors should bring to mind the possibility of an abdominal pregnancy. In the management of such a pregnancy if the placenta is so situated that it can be easily removed, without damage to vital structures or undue consumption of time and when the circulation can be easily and completely controlled, this should be done and the abdomen closed without drainage. If easy removal is not possible or probable, no attempt should be made to remove the placenta, and again the abdomen should be closed without drainage. Marsupialization of the placenta or drainage of the abdomen with the placenta left in appears to be the worst treatment of all. Necrosis of the placenta and membranes is a physiologic process and should not of itself be an indication for drainage. Mortality (14.3 per cent in the series of Cornell and Lash and 18.8 per cent in the present sixty-nine cases) and morbidity rates for the condition are much higher than they need be. Earlier recognition by having the possibility in mind, dangerous and futile attempts to "induce labor" and better surgical judgment at the time of operation, chiefly in regard to management of the placenta, should lower the mortality rate.

American Journal of Ophthalmology, St. Louis

23:617-734 (June) 1940

- Ocular Complications of Meningococcic Meningitis: Observations in 350 Cases. P. M. Lewis, Memphis, Tenn.—p. 617.
Studies on Infectivity of Trachoma: X. Frequency and Distribution of Inclusion Body and Its Possible Relation to Pathogenesis. L. A. Julianelle, St. Louis.—p. 633.
Essential Progressive Atrophy of Iris: Report of Case. J. W. Henderson and W. L. Benedict, Rochester, Minn.—p. 644.
The American Board of Ophthalmology. W. B. Lancaster, Boston.—p. 651.
Field Changes After Satisfactory Filtration Operations for Glaucoma. J. W. Burke, Washington, D. C.—p. 657.
Sulfanilamide and Neoprontisol in Treatment of Trachoma. R. D. Harley, A. E. Brown and W. E. Herrell, Rochester, Minn.—p. 662.
Edward Delafield: A Sketch. B. Samuels, New York.—p. 670.
*Treatment of Trachoma with Sulfanilamide: Report of Thirty-One Cases. P. Thygeson, New York.—p. 679.

Sulfanilamide in Trachoma.—Thygeson reports that, since March 1938, all trachoma patients seeking treatment at the Vanderbilt Clinic and Institute of Ophthalmology have received sulfanilamide. Of thirty-one who have completed their course sixteen were healed, eleven showed satisfactory improvement and four exhibited little or no change. The drug appeared to be most efficacious in the early cases and when employed in relatively high dosages, but healing was obtained in long-standing cicatricial cases and in some in which low doses were given over a relatively long period. Sulfanilamide effected rapid disappearance of the epithelial cell inclusions characteristic of active trachoma but seemed to have little influence on secondary bacterial infection caused by *Haemophilus influenzae*, *Diplococcus pneumoniae* or *Staphylococcus aureus*. Corneal lesions responded more rapidly than the conjunctival, and papillary hypertrophy regressed much more rapidly than follicular hypertrophy.

American Journal of Physiology, Baltimore

129:227-504 (May) 1940. Partial Index

- Radioactive Phosphorus as Tracer in Anaerobic Muscular Contraction. J. Sacks, Ann Arbor, Mich.—p. 227.
Cyclic Penetrability of Human Cervical Mucus to Spermatozoa in Vitro. J. K. Lamar, L. B. Shettles and Eleanor Delfs, Baltimore.—p. 234.
Relation of Plasma Potassium Level to Metabolic Activity. G. Brewer, Philadelphia.—p. 245.
Renal Excretion of Sucrose in Normal Man; Comparison with Inulin. K. Steinitz, Istanbul, Turkey.—p. 252.
Effects of Adrenalin on Tubal Contractions of Rabbit in Relation to Sex Hormones (Study in Vivo by Rubin Method). A. M. Davids and M. B. Bender, New York.—p. 259.
Effect of Changes in Muscle Electrolyte on Response of Skeletal Muscle to Tetanic Stimulation, with Particular Reference to Potassium. H. C. Miller and D. C. Darrow, New Haven, Conn.—p. 264.
Changes in Cholesterol Content of Hepatic Bile Subjected to Gallbladder Activity. Cecilia Riegel, D. G. Calder and I. S. Ravdin, Philadelphia.—p. 271.
Action of Osmotically Active Substances on the Heart Rate. C. R. Spelman.—p. 293.

American Journal of Public Health, New York

30:463-588 (May) 1940

- Dust Control in Rock Drilling. L. Greenburg, T. F. Hatch, W. J. Burke and W. B. Harris, New York.—p. 463.
- Automatic Control of Pasteurization: Advantages and Safeguards. A. W. Fuchs, Washington, D. C.—p. 477.
- Evaluation of Cancer Control Methodology. Eleanor J. Macdonald and Frances A. Macdonald, Boston.—p. 483.
- Integrating Industrial Hygiene with Local Health Service. L. M. Graves, A. H. Fletcher, Memphis, Tenn.; and C. Pharris, Nashville, Tenn.—p. 493.
- Suggested Grouping of Slow Lactose Fermenting Coliform Organisms. C. A. Stuart, Providence, R. I.; F. L. Mickle and E. K. Borman, Hartford, Conn.—p. 499.
- Jaundice in Detroit. J. G. Molner and K. F. Meyer, San Francisco.—p. 509.
- Community Health Education. I. V. Hiscock, New Haven, Conn.—p. 516.
- Healthier Health Meetings. W. W. Bauer, Chicago.—p. 523.
- Some Developments in the Water Pollution Research Program of the Public Health Service. J. K. Hoskins, Cincinnati.—p. 527.
- Weekly and Seasonal Trends of Upper Respiratory Infections in Group of 2,000 Students. F. Sargent, Cambridge, Mass.—p. 533.
- *The Problem of the Gonococcus Carrier. C. M. Carpenter and R. S. Westphal, Rochester, N. Y.—p. 537.
- Staff Education Through Study of Malnutrition in School Children. G. M. Wheatley, Astoria, N. Y.—p. 542.

The Gonococcus Carrier.—Carpenter and Westphal investigated the duration of the gonococcus carrier state of 1,061 inmates of a penal institution. The inmates were under rigid supervision and their period of incarceration was long enough to make the observations significant. Of the 937 white males 330 (35 per cent) had gonococcal infection and of the 124 Negroes sixty-two (50 per cent) gave a positive history. Not a single case of acute infection was observed during the nine months of the study. Eleven carriers of the gonococcus were disclosed, all white men. Three patients had symptoms of gonococcal infection and eight presented clinical evidence of the disease. *Neisseria gonorrhoeae* was isolated in culture from each carrier. Smears were negative in every instance except one. The cultures were recovered from urethral exudate, prostatic secretion and/or urinary sediment. Strains of *Neisseria pharyngis sicca* and *Neisseria catarrhalis* were isolated from the genito-urinary tract of two of the carriers and thirteen other men. Physical examination revealed no anatomic or clinical signs that explained why the eleven carriers continued to harbor the gonococcus. The longest proved carrier state was seven years and two months. The importance of accurate laboratory methods of diagnosis cannot be overemphasized.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

43:629-804 (May) 1940

- Malignant Tumors of Kidney in Adults. C. L. Gillies, Iowa City.—p. 629.
- Anomalies of Urinary Tract. W. J. Baker, Chicago.—p. 636.
- Ureteral Obstruction. B. H. Nichols, Cleveland.—p. 649.
- Pleurovenous Backflow. W. L. Kilby, Baltimore.—p. 659.
- Lateral Pyelography. E. L. Shiffett and D. Y. Keith, Louisville, Ky.—p. 664.
- Calculus in Urachus: Report of Case with Enuresis. G. M. Wyatt and T. H. Lanman, Boston.—p. 673.
- Pulmonary Lesions After Roentgen and Radium Irradiation. R. B. Engelstad, Oslo, Norway.—p. 676.
- *Radiation Reaction in Lung. S. Warren and J. Spencer, Boston.—p. 682.
- Primary Lymphosarcoma of Hard Palate. L. J. Freedman, New York.—p. 702.
- Carcinoma of Anus. O. N. Meland, Los Angeles.—p. 706.
- Surface Applications of Radon in Rectal Cancer. G. E. Binkley, New York.—p. 711.
- Carcinoma of Colon (Exclusive of Rectum). W. M. Shedden and R. Dresser, Boston.—p. 715.
- Cathode Rays for Radiation Therapy. J. G. Trump, R. J. Van de Graaff and R. W. Cloud, Cambridge, Mass.—p. 728.
- Comparative Roentgen Ray Diffraction Study of Several Natural Apatites and Apatite-like Constituent of Bone and Tooth Substance. W. F. Bale, Rochester, N. Y.—p. 735.

Radiation Reaction in Lung.—Warren and Spencer reviewed 398 cases of tumors situated between the diaphragm and the neck in the Huntington, Deaconess and Pondville hospitals for evidence of irradiation pneumonitis. Necropsy was performed in all; 234 had received some irradiation over the thorax and 163 had not. The amount of irradiation varied from 800 to 15,000 roentgens; a few cases of breast cancer had

implantation of radium needles only. The points used to differentiate irradiation reaction from other inflammatory changes in lungs were: (1) a hyaline membrane closely adherent to the alveolar walls and always associated with one or all of the following changes, (2) swollen alveolar lining cells either with or without desquamation and fibrosis, edema or mild inflammatory exudation in the supporting tissue, (3) edema without appreciable inflammatory reaction, (4) diffuse alveolar fibrosis without evidence of organizing pneumonia, tuberculosis or silicosis, (5) an unusual fibrillar hyalinization of the alveolar walls, (6) hyalinization of the arterial walls and (7) interalveolar capillary changes; swelling of endothelium and thrombosis. The interval from irradiation to death in large part determined the type of reaction, explaining the absence of reaction in some patients who had received large amounts of radiation. The frequency of pulmonic change increased as did the amount of radiation but not with any regularity. The majority of the cases showing irradiation reaction had an unproductive hacking cough during the height of the local cutaneous reactions. The tissue changes following irradiation of the lungs varied with the amount and kind of radiation. It is probable that the earliest effect is one of mild injury to the alveolar lining cells and the capillary endothelium. Edema, swelling, necrosis and proliferation of the endothelium and alveolar epithelium follow. With injury to connective tissue, fibroblastic proliferation, chiefly in the alveolar walls, occurs. Peribronchial, septal or pleural fibrosis has not been specifically identified with irradiation pneumonitis. Appreciable injury and repair of fibrous tissue occurred only after intensive irradiation. It is not possible to distinguish early acute irradiation pneumonitis from other conditions, although prominent edema and large epithelial and endothelial cells in the absence of much exudate are suggestive. When the primary injury is sufficiently severe to affect the endothelium, fibrous tissue and epithelium, the well developed repair process resembles that following injurious agents. Fibrous thickening and hyaline swelling of veins and arteries associated with irradiation pneumonitis are seen occasionally in youth and more commonly with advancing age, frequently unaccompanied by other disease processes. These changes may be restricted to that portion of the lung which presents other evidence of irradiation pneumonitis and which is known to have been included in the field of irradiation. The only microscopic sign that can with certainty be recognized as irradiation pneumonitis is that which shows some degree of both the early and late stages in the same lung. The hyaline membrane probably represents an acute or subacute response and is diagnostic of irradiation pneumonitis. The other changes are less distinctive and not as easily differentiated from infectious processes.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

24:265-400 (May) 1940

- Untoward Reactions of Tryparsamide. I. Kopp and H. C. Solomon, Boston.—p. 265.
- Statistical Studies of Serologic Surveys. R. Ledgerwood, Springfield, Ill.—p. 284.
- Hemolyzed Beef Blood or Sheep Blood Mediums for Isolation of Gonococcus. A. Cohn and Ruth G. Kruger, New York.—p. 295.
- Liver Damage After Recovery from Postarsphenamine Jaundice: Follow-Up Study. T. J. Rankin, Cincinnati, and F. W. Marlow Jr., Boston.—p. 301.
- Supposed Daily Variation of Reagin Content of Syphilitic Serum. C. F. Mohr and C. A. Smith, Baltimore.—p. 322.
- Acute Necrosis of Liver in Infants Following Sodium Bismuth Thioglycollate Administration. I. J. Wolman, Philadelphia.—p. 330.
- Sulfanilic Sulfanilamide (Disulon) in Treatment of Gonococcal Urethritis and Its Complications. H. W. Berg, Albany, N. Y.—p. 337.
- *Use of Disulfanilamides in Gonorrhea. S. A. Vest and D. S. Parker Jr., Baltimore.—p. 344.
- Classification of Rectal Strictures Due to Lymphogranuloma Venereum. T. R. Peyton, Philadelphia.—p. 360.
- Joseph Grünpeck's Libellus de Mentulagra Alias Morbo Gallico of 1503. E. L. Zimmermann, Baltimore.—p. 364.

Disulfanilamides for Gonorrhea.—Vest and Parker compared the effect of sulfanilic sulfanilamide and the sodium salt of its derivative sulfanilic dimethyl-sulfanilamide in sixty cases of gonorrheal urethritis. Patients were treated solely with these drugs without local irrigations. Sulfanilic sulfanilamide in the dosage (1.6 Gm. daily) used has shown considerable antigon-

orrhoeal activity. Larger doses would probably give superior results, although the possibility of peripheral neuritis might be enhanced. The dimethyl derivative, uliron, has shown but little antigonorrhoeal activity in the dosage (3 Gm. daily) and regimen in which it was administered. There were few disagreeable toxic symptoms after uliron; paralysis of the thumb developed in one patient, while another had a severe cutaneous rash. Unpleasant symptoms, principally nausea, diarrhea and severe muscular pains (occurring less often than with sulfanilamide) occurred a number of times with sulfanilyl sulfanilamide. The muscular pains may have been prodromal of neuritis. Sulfanilyl sulfanilamide has been valuable in sulfanilamide-resistant cases and in selected cases of gonorrhoeal urethritis. Sulfanilyl dimethyl-sulfanilamide was inferior to either sulfanilyl sulfanilamide or sulfanilamide in the treatment of gonorrhoea in the dosage scheme used by the authors. It does not exert a profound influence on the course of the disease, is not without dangerous toxic potentialities and is accompanied by a high incidence of gonorrhoeal complications.

Annals of Internal Medicine, Lancaster, Pa.

13:2025-2204 (May) 1940

- Effect of Specific Agents Extracted from Soil Micro-Organisms on Experimental Bacterial Infections. R. J. Dubos, New York.—p. 2025.
- *Comparative Effectiveness and Toxicity of Sulfathiazole and Sulfapyridine in Pneumococcal Pneumonia. H. F. Flippin, L. Schwartz and S. B. Rose, Philadelphia.—p. 2038.
- Studies in Mucous Membrane Hypersensitiveness: IV. Allergic Reaction in Passively Sensitized Mucous Membranes of Ileum and Colon in Humans. I. Gray, M. Harten and M. Walzer, Brooklyn.—p. 2050.
- Visceral Syndrome: New Concept of Visceromotor and Sensory Changes in Relation to Deranged Spinal Structures. N. T. Ussher, Santa Barbara, Calif.—p. 2057.
- Calcereous Aortic Stenosis: Report of Nine Cases with Autopsy Findings. L. Cohen, I. Gray, P. I. Nash and H. Fink, Brooklyn.—p. 2091.
- Determination of Biliary Tract Infection with Encapsulated Duodenal Tube. J. R. Twiss, R. F. Carter and R. Hotz, New York.—p. 2104.
- *Hormone Therapy for Treatment of Hirsuties: Preliminary Report. G. B. Dorff, Brooklyn.—p. 2112.
- Pseudomegacolon. A. Oppenheimer, Beirut, Lebanon, Syria.—p. 2128.
- Popularity of Ewald-Boas Test Meal; Reasons for Its Survival. D. Sandroni and Z. Sagal, New York.—p. 2134.
- Some Observations on Persistence of Bachman Skin Test and of Eosinophilia After Recovery from Trichinosis. M. Warren, E. H. Drake and R. S. Hawkes, Portland, Maine.—p. 2141.
- Use of Histamine in Rheumatoid Arthritis. R. O. Muether, St. Louis.—p. 2147.
- Subacute Bacterial Endocarditis in Older People. T. B. Bayles and W. H. Lewis Jr., New York.—p. 2154.
- *Simmonds' Disease (Pituitary Cachexia): Report of Case. J. E. Farber, Buffalo.—p. 2171.

Sulfathiazole and Sulfapyridine in Pneumonia.—Flippin and his associates studied the first hundred pneumonia patients treated with sulfathiazole and an equal number treated with sulfapyridine for a comparison of the effectiveness and toxicity of the two drugs. Of the 200 patients, nineteen (ten sulfathiazole, nine sulfapyridine) received specific antipneumococcus serum in addition to chemotherapy. Serum was given when sulfathiazole or sulfapyridine had apparently failed to bring about the expected clinical response within thirty-six to forty-eight hours. Twelve treated with sulfathiazole and fifteen treated with sulfapyridine died. Five patients moribund on admission were treated with sulfathiazole and four with sulfapyridine. If these cases are excluded the corrected mortality becomes 7.4 and 11.4 per cent respectively for the sulfathiazole and sulfapyridine treated groups. Thirteen patients with bacteremia were treated with sulfathiazole and four of these died. Three of these died within twenty-four hours. Six of the eleven bacteremic patients in the sulfapyridine treated group died. Three of these patients also died within twenty-four hours. In both groups the unusually high incidence of type III infection has probably raised the mortality. Of ten type III deaths, four were twenty-four hour deaths. Therefore the corrected mortality values are less affected by the high incidence of this type of infection. A greater number of patients treated with sulfathiazole received treatment during the first three days of the disease but this did not have a decided influence on the comparative mortality rates of the two groups. Of the twelve fatal cases treated with sulfathiazole, seven were treated after the third day of the disease and four of the deaths occurred

within twenty-four hours after admission. In the sulfapyridine treated group eight of the fifteen deaths occurred in patients treated after the third day of the disease and five of these died in less than twenty-four hours after admission. Sulfapyridine brought the temperature down somewhat more rapidly than sulfathiazole, although the average number of hospital days (13.2) for the two groups was the same. Complications were approximately the same in the two groups of patients. Nausea and vomiting were much less marked in frequency and severity in the sulfathiazole group, as were other toxic manifestations. The value of combined drug and serum therapy is questionable at present, but until sufficient data are presented to prove it definitely less effective than chemotherapy alone the authors believe in the combined use of serum and drug in selected cases. It is their impression that the administration of serum was a deciding factor in the recovery of several patients.

Endocrine Therapy for Hirsuties.—Dorff used theelin by injection in eight cases of female hirsuties and by hypodermic administration in others. The gonadotropic factor of the anterior pituitary gland was used in some in an attempt to stimulate the ovary directly. The eight patients, from 15 to 23 years of age, presented no definite neoplastic pathologic changes in the adrenal, ovary or pituitary glands on clinical examination. All the patients showed some signs of masculinization; hirsuties of the face, trunk and extremities, heterologous formation of suprapubic hair, some exaggeration of the size of the clitoris and irregular or scanty menstrual periods of five patients. Although endocrine therapy did not completely eradicate the hirsuties, it provoked enough important changes to lead one to believe that it might be a stepping stone toward improved therapy; for after treatment had been administered for a time some of the superfluous hairs on the cheeks, chin, parts of the thighs and legs fell out spontaneously. In addition the superfluous hair which had not fallen out became loosened at its roots. In several of the patients there was a familial tendency to superfluous hair growth. However, in spite of this apparent hereditary factor the response to endocrine treatment was the same as in patients with no such tendency. The good effects on hirsuties were comparatively short lived. Within a period ranging from several weeks to several months regrowth began. However, with this regrowth the new hair no longer appeared in its original stubborn or coarse state but was of a lighter color and finer texture and it appeared in a more loosely rooted state so that it could be plucked with ease. While all these changes were taking place in the hirsute areas the normal hair did not fall out nor did it ever loosen. In addition to changes in the hirsutism the menstrual irregularity tended toward correction in some of the patients. The general psychic outlook of most of the patients was greatly improved and a certain feminizing effect was reflected in the facial appearance and demeanor of most of them after treatments had been in progress for a time. Oral administration of a placental extract, emmenin, was given in two cases in addition to local and hypodermic estrogen therapy. With this addition in one case, even though previous theelin therapy provoked no beneficial change, some of the facial hair loosened and fell out. In the other case a falling out and loosening of the hair occurred so that it could be plucked easily, eliminating the necessity of shaving.

Simmonds' Disease.—Farber observed a patient with a clinical diagnosis of pituitary cachexia for two years. The diagnosis was subsequently verified at postmortem examination. The significant clinical symptoms and signs were cachexia, blindness, loss of axillary and pubic hair, atrophy of the breasts and genitalia, amenorrhoea, asthenia, anorexia and constipation, integumentary changes, hypotension, hypothermia, oligodipsia, oliguria, mental changes and pathologic sleep. Laboratory studies showed a lowered basal metabolic rate, lowered or depressed specific dynamic action of proteins, hypoglycemia, decreased dextrose tolerance, hypocholesterolemia, hypochloremia and hypochloruria, anemia and relative lymphocytosis, and disturbed water and salt balance. It was felt that the mental changes, pathologic sleep, hypothermia, disturbances in water and salt balance and the blindness were probably due to injury by the expanding tumor into surrounding structures, especially

the optic nerves and hypothalamus. Replacement therapy and exploratory craniotomy were unsuccessful. At autopsy a pituitary stalk tumor (cystic epithelioma) was found. There was a generalized microsplanchnia.

Archives of Ophthalmology, Chicago

23:1131-1392 (June) 1940

- Ocular Manifestations in Hydroa Vacciniforme. W. H. Stokes, Omaha.—p. 1131.
- Measurement of Structures of Fundus: Presentation of Improved Technic. J. M. Cotton and S. Rosin, New York.—p. 1146.
- Retrolental Tissue from Choroid in Kuhl-Junius Degeneration of Macula: Anatomic Study. E. V. L. Brown, Chicago.—p. 1157.
- Paradoxical Monocular Ptosis. T. R. Yanes, Habana, Cuba.—p. 1169.
- Subconjunctival Lagrange Sclerectomy ab Externo. R. J. Curdy, Kansas City, Mo.—p. 1173.
- Comments on Teaching of Refraction. B. Friedman, New York.—p. 1175.
- Shortening of Eyeball for Retinal Detachment. W. E. Borley, San Francisco.—p. 1181.
- Congenital Retinal Fold. F. H. Theodore and J. Ziporkes, New York.—p. 1188.
- Glaucoma Following Irradiation: Pathologic Report. L. Bothman, Chicago.—p. 1198.
- Melanosarcoma of Choroid: Report of Case with Unusual Features. E. N. Beery, Brooklyn.—p. 1213.
- Further Evidence of Change in Position of Eyeball During Fixation. G. E. Park, Chicago, and R. S. Park, Richmond, Ky.—p. 1216.
- Hypertrophy of Thymus in Vernal Conjunctivitis. G. Alamilla, Habana, Cuba.—p. 1231.
- Effects of Sulfanilamide and Sulfapyridine on Koch-Weeks Bacillus (Haemophilus Influenzae). J. S. Guyton, Baltimore.—p. 1243.
- Gyrate Atrophy of Retina and Choroid Following Retinitis Pigmentosa: Report of Two Cases. W. T. Davis and E. Sheppard, Washington, D. C.—p. 1252.
- Retinitis Pigmentosa: Etiologic and Clinical Implications Based on Twenty-One Cases. R. C. Moehlig and R. H. Pino, Detroit.—p. 1257.
- Tonic Deviations of Eyes Produced by Movements of Head, with Special Reference to Otolith Reflexes: Clinical Observations. F. R. Ford and F. B. Walsh, Baltimore.—p. 1274.
- Choroideremia. B. Friedman, New York.—p. 1285.
- Pulsating Exophthalmos. H. S. Sugar and S. J. Meyer, Chicago.—p. 1288.

Archives of Otolaryngology, Chicago

31:711-884 (May) 1940

- Endaural Fenestration of External Semicircular Canal for Restoration of Hearing in Cases of Otosclerosis: Summary Report of 120 Cases. J. Lempert, New York.—p. 711.
- *Diagnosis and Treatment of Carcinoma of Lung, with Statistical Review of Forty Cases. A. E. Hammond, Detroit.—p. 780.
- Sulfanilamide in Treatment of Acute Infection of Ear and of Mastoid in Infants and in Children: Quantitative Study of Seventeen Cases. H. M. Hebble, Philadelphia.—p. 808.
- Significance of Aphasia as Symptom of Otogenic Extradural Abscess. F. Altmann, New York.—p. 819.
- Plastic Operations for Hump Nose: Notes on Artistic Anatomy. A. M. Brown, Chicago.—p. 827.
- Osteoma of the Mastoid: Report of Case with Investigation of Constitutional Background. E. A. Stuart, Montreal.—p. 838.

Carcinoma of Lung.—Hammond presents a detailed study of forty cases of carcinoma of the lung. The ratio of men to women was 4:1. The higher rate in men is explained on the basis of the excessive use of tobacco, the tar from the combustion acting as a carcinogenic element. Other irritative elements, chemical, mechanical, bacterial, thermal and radioactive agents, may also contribute. The highest age incidence (72.5 per cent) was between 40 and 60 years. The most important clinical symptoms were cough, pain, loss of weight, hemoptysis, dyspnea and hoarseness. Cough occurred in 100 per cent and hoarseness in 10 per cent; the remaining symptoms occupied positions between the two. Bronchoscopic study was the sole and indisputable diagnostic procedure in nearly all cases. Physical signs and x-ray studies were of little value. The malignant grade of the carcinoma was of little value in estimating the final outcome in the individual case. None of the six patients operated on survived for as long as nine months. Of the twenty-six patients treated by irradiation, four apparently have been cured and for the others some prolongation of life with more or less satisfactory palliation was obtained. The patients apparently cured were in the early stage, and the good results were obtained by the combination of roentgen irradiation administered externally and radium intrabronchially. The treatment of this dreaded disease constitutes a problem whose solution is still in the future.

Archives of Physical Therapy, Chicago

21:257-320 (May) 1940

- Comparison of Treatment of Severe Asthma by Electrophoresis of Epinephrine with Other Methods. H. A. Abramson, New York.—p. 261.
- Evaluation of Some Methods of Treatment in Peripheral Vascular Disease. W. Bierman, New York.—p. 267.
- *Management of Facial Paralysis by Physical Measures. M. K. Newman, J. M. Berris and S. S. Bohn, Detroit.—p. 270.
- *Modified Rapid Sinusoidal Current for Trigeminal Neuralgia: Supplementary Report of 100 Additional Cases. B. Uianski, Philadelphia.—p. 275.
- Postural Reflexes. O. L. Huddleston, Denver.—p. 282.
- Individual Play Exercises for Handicapped Children. Bertha Weinmann, Chicago.—p. 289.
- Further Studies in Electrosurgical Management of Retinal Separation. O. B. Nugent, Chicago.—p. 297.
- Advantages of Institutional Care and Physical Therapy in Chronic Arthritis. J. F. Wyman, Milwaukee.—p. 301.

Management of Facial Paralysis by Physical Measures.—Newman and his co-workers state that the treatment of facial paralysis is dependent on its various etiologic factors, on the question of whether the paralysis is of central or peripheral origin, and on the site of the lesion. They managed thirty cases by the use of physical therapeutic measures. The ages of the patients ranged between 6 and 79 years, average 37. With the onset of an acute refrigerans type of facial paralysis iodides in saturated solution of potassium or syrup of hydriotic acid are indicated for their general alterative action. Analgesics are valuable. Saline laxatives are used during the acute stage of inflammation for their possible detergent effect. The physical measures applicable during the acute phase of the refrigerant palsies are directed toward the reduction of the inflammatory exudate and toward keeping the denervated muscles in position of physiologic rest. Decongestion at the stylomastoid foramen can be accomplished by cantharides plasters, hot moist applications, radiant heat, negative galvanism and conventional or short wave diathermy. The frequency of application is indicated by the pain and the tolerance of the tissues. To prevent muscles from stretching they are supported by attaching two Y bands of adhesive tape at the zygomatic bone and temporal region. Positive galvanism is especially efficacious for the relief of pain. With the subsidence of the acute symptoms within eight to ten days, testing for reaction of degeneration is instituted. When no reaction of degeneration is present, recovery can be expected in from two to eight weeks. If a sufficient amount of recovery is not obtained after six months of rigorous physical therapeutic measures, surgery is to be considered. Active treatment now consists of heat, massage, voluntary exercise and electrical stimulation (with interrupted galvanic, sinusoidal and faradic currents). Diathermy or radiant heat is applied to the paralyzed side of the face for from fifteen to thirty minutes. Another method of promoting a circulatory response consists of the common ion transfer 0.5 per cent acetyl-beta-methylcholine hydrochloride. From 15 to 20 milliamperes of the galvanic current for twenty minutes is adequate. Negative galvanism for its heating effect can be applied for thirty minutes over the stylomastoid foramen. The strength of current should be just less than the amount required to cause a contraction of the muscles on the unaffected side. On the first day three contractions over the motor points are sufficient, and on subsequent days the number of contractions is increased but always kept within the fatigue range of the muscle. After one or two weeks the slow sine wave is substituted, from twenty to thirty contractions per minute being used. When the faradic current can be tolerated, it should replace the sine wave current. Gentle stroking massage which follows stimulation preserves muscular tone. Exercise of the facial muscles is carried out in front of a mirror every day. The etiologic agent must always be removed before physical measures are instituted. Seventeen of the thirty cases followed exposure, six middle ear disease, one dental manipulation, one trauma associated with an automobile accident, two head colds, one mumps, one an operation on the eighth nerve for vertigo, one a postpartum infection and two mastoidectomy. In the seventeen cases of exposure paralysis, a partial reaction of degeneration or no reaction of degeneration was present after ten days. Eight of these patients

received only heat, massage and exercise, while the remainder received electrical stimulation as well.

Sinusoidal Current for Trigeminal Neuralgia.—Ulanski reports 100 additional cases which supplement sixty-five cases of trigeminal neuralgia reported in 1937 and treated by a modified rapid sinusoidal current. In the last seventy-five cases the current used was further changed to one of 43,200 alternations per minute. This modification has produced a smoother current, has added to the beneficial results obtained and has lessened the amount of discomfort to the patient while under treatment. Of the last 100 patients immediate relief was obtained by 85 per cent; 50 per cent of these patients have been free from pain for from one to six years. Two had recurrence of symptoms but additional treatment again relieved them. The advantages of the modified sinusoidal treatment of trigeminal neuralgia are that typical and atypical cases can be treated at the office or the patient's home, there are no after-effects (sensory or motor disturbances), the method can be used regardless of any other previous treatment, there are no contraindications and all divisions of the nerve can be treated.

Archives of Surgery, Chicago

40:1039-1218 (June) 1940

- General Principles of Preoperative and Postoperative Treatment. A. Blalock, Nashville, Tenn.—p. 1039.
 Preanesthetic Medication. B. H. Robbins, Nashville, Tenn.—p. 1044.
 Preoperative and Postoperative Treatment of Patient with Diabetes. L. S. McKittrick and H. F. Root, Boston.—p. 1057.
 Preoperative and Postoperative Care of Patients with Lesions of Stomach and Duodenum. W. Walters and H. R. Hartman, Rochester, Minn.—p. 1063.
 Preoperative and Postoperative Treatment of Patients with Lesions of Small Intestine and Colon. J. R. Paine, Minneapolis.—p. 1083.
 Effect of Diet on Composition of Liver in Presence of Obstruction of Common Bile Duct. J. Johnson, I. S. Ravdin, H. M. Vars and H. A. Zintel, Philadelphia.—p. 1104.
 Preoperative and Postoperative Care in Anorectal Surgery. L. A. Buie, Rochester, Minn.—p. 1116.
 Preoperative and Postoperative Treatment of Toxic Goiter. N. A. Womack, St. Louis.—p. 1123.
 Preoperative and Postoperative Care of Patients with Surgical Diseases of Chest. J. Alexander, Ann Arbor, Mich.—p. 1133.
 Preoperative and Postoperative Care of Patients with Lesions of Heart and Pericardium. C. S. Beck, Cleveland.—p. 1151.
 Preoperative and Postoperative Management in Gynecology. G. H. Gardner, Chicago.—p. 1164.
 Preoperative and Postoperative Care in Neurosurgical Procedures. C. Pilcher, Nashville, Tenn.—p. 1176.
 Preoperative and Postoperative Treatment in Urology. C. Huggins and C. Vermeulen, Chicago.—p. 1185.
 Preoperative and Postoperative Care in Reconstructive Surgery. J. B. Brown, L. T. Byars and F. McDowell, St. Louis.—p. 1192.

Canadian Medical Association Journal, Montreal

42:413-520 (May) 1940

- Mammary Tumors Produced in Rats by Action of Estrone Tablets. R. L. Noble, C. S. McEuen and J. B. Collip, Montreal.—p. 413.
 Blood Group Classifications (Plea for Uniformity). I. H. Erb, Toronto.—p. 418.
 Compression Fractures of Os Calcis. G. Murray, Toronto.—p. 422.
 Renal Tuberculosis. H. D. Morse, Winnipeg, Man., and D. L. Scott, Ninette, Man.—p. 424.
 Epithelioma of Limbus. E. P. Grenier, Montreal.—p. 428.
 Pollen Survey in Manitoba. C. H. A. Walton and Margaret G. Dudley, Winnipeg, Man.—p. 430.
 Cyclopropane—Unmixed. B. C. Leech, Regina, Sask., and H. R. Griffith, Montreal.—p. 434.
 Treatment of Diabetes in Children. Gladys Boyd, Toronto.—p. 438.
 Treatment of Placenta Praevia. W. A. Scott, Toronto.—p. 442.
 Treatment of Puerperal Sepsis. L. T. Armstrong, Toronto.—p. 445.
 Intussusception. D. S. Macnab, Calgary, Alta.—p. 447.
 How To Be Wrong: The X-Ray, a Quick and Easy Method. H. W. Schwartz, Halifax, N. S.—p. 450.
 Treatment of Nasal Sinus Infection by Ultra Short Wave Diathermy. W. P. E. Paterson, Ottawa, Ont.—p. 454.
 Some Fundamental Principles in Treatment of Skin Disorders. G. B. Sexton, London, Ont.—p. 457.
 Recurrent Pneumococcal Meningitis Complicating Skull Fracture. A. R. Elvidge and E. Roseman, Montreal.—p. 460.

Florida Medical Association Journal, Jacksonville

26:529-580 (May) 1940

- Appendicitis. L. M. Gable, St. Petersburg.—p. 545.
 Multiple Blood Transfusions in Acute Leukopenia of Adult Lobar Pneumonia. E. Evans and B. F. Hart, Winter Park.—p. 551.
 The Cross-Eyed Child. N. S. Rubin, Pensacola.—p. 555.

Georgia Medical Association Journal, Atlanta

29:251-294 (May) 1940

- Medicine: Yesterday and Tomorrow. W. H. Myers, Savannah.—p. 251.
 Postoperative Care. J. G. McDaniel, Atlanta.—p. 255.
 *Chronic Brucellosis: Report of Two Cases in Children Diagnosed by Intracutaneous Tests. Helen W. Bellhouse, Thomasville.—p. 260.
 Recent Advances in Treatment of Mental Disorders. J. N. Brawner and A. F. Brawner, Smyrna.—p. 264.
 Etiologic Factors of Sterility in the Male: Report of Case. C. Rieser, Atlanta.—p. 269.
 Founding of the Southern Medical College: Events Preceding Its Organization. G. Murphy, Atlanta.—p. 273.
 Gonococemia: Patient Unsuccessfully Treated with Sulfanilamide. J. F. Schneider and J. C. Massee, Atlanta.—p. 276.

Chronic Brucellosis.—Bellhouse points out that symptoms of chronic undulant fever are varied and kaleidoscopic and range from the acute, febrile illness of twelve days, which in a child could be called almost anything, through more protracted acute illness with typical remissions, to the protracted mild illness with symptoms of occasional elevation of temperature and fairly consistent anorexia, increased irritability and nervousness, occasional sweating and vague joint pains. Undulant fever is poorly recognized in infants in countries in which it is endemic, and this is even more likely to occur with abortus infections, which produce, as a rule, milder more chronic illnesses in which the physician is less likely to avail himself of the proper laboratory procedures. This is particularly true in infants and small children. In addition to the cutaneous tests, agglutination tests and routine blood cultures should be done. Children might be more susceptible to brucella infection than is generally suspected and the disease might fail to be recognized because it occurs in a mild, obscure form without development of agglutinins. The biologic immaturity of the tissues of the younger child may explain the difference in the immune reactions. Two cases in children are reported whose clinical histories together with positive cutaneous tests enabled the author to make a definite diagnosis of chronic brucellosis, probably of three years' duration. The strongly positive cutaneous reactions became minimal in two and one half months, during which time the children had no common change of regimen except that they had been given pasteurized instead of raw milk. Agglutination tests, as is frequently the case in children, had proved of no value in diagnosis. A positive intracutaneous test alone is not sufficient. It merely signifies exposure and sensitization and should be correlated with the clinical history and other accepted tests. Cattle should be tested in a routine manner for all types of Brucella.

Iowa State Medical Society Journal, Des Moines

30:229-272 (June) 1940

- Medicine and Public Relations. F. A. Hennessy, Calmar.—p. 229.
 Some Methods of Stimulating Medical Progress in Iowa. F. P. McNamara, Dubuque.—p. 233.
 Present Status of Knowledge of Whooping Cough. E. N. Hesbacher, Des Moines.—p. 236.
 Intravenous Anesthesia and Its Uses. F. J. Piekenbrock and P. F. Olson, Dubuque.—p. 240.
 Plasma Proteins in Surgery. E. S. Korfmacher, Grinnell.—p. 242.

Journal of Allergy, St. Louis

11:333-438 (May) 1940

- Inquiry into Reagents in Convalescent Serum Indicating Its Inhibiting Effect. I. H. Tumpeer and E. Rubens, Chicago.—p. 333.
 Subcutaneous Tissue Pressure Studies in Urticaria and Angioneurotic Edema. W. T. Vaughan and D. M. Pipes, Richmond, Va.—p. 349.
 Summer Hay Fever of Unknown Origin in the Southeast. C. K. Weil, Montgomery, Ala.—p. 361.
 *May Fly (Ephemera) Hypersensitivity. K. D. Figley, Toledo, Ohio.—p. 376.
 *Use of Potassium Chloride in Treatment of Allergic Conditions. W. C. Spain, F. H. Westcott and G. E. Gaillard, New York.—p. 388.

May Fly (Ephemera) Hypersensitivity.—Figley states that May fly hypersensitivity is quite common among allergically susceptible individuals exposed to these insects by reason of their residence near the Great Lakes or other large fresh water bodies. Persons with symptoms of seasonal hay fever and asthma should always be tested for May fly sensitization. Among 1,284 patients with seasonal hay fever and pollinosis who were adequately tested the author found that ninety-five (7.4 per cent) reacted to May fly. Of these, twenty reacted to May fly alone and twenty to May fly and some other inhalant, usually ragweed pollen. That the other fifty-five

patients were specifically sensitive is shown by the fact that many of them were tested by passive transfer or by inhalation of powdered May fly and all reacted positively. These fifty-five patients had all been exposed more than once to May fly contact and had developed specific hypersensitivity. They were not treated with May fly because they lived inland and could avoid exposure. The first forty patients were all treated with extracts of May fly or of May fly and ragweed pollen, with satisfactory results.

Potassium Chloride for Allergic Conditions.—According to Spain and his associates, the effect of potassium chloride medication on allergic conditions was disappointing. Of fifteen patients with hay fever who received potassium chloride alone, twelve obtained no relief. Not only was the date of onset not delayed but the severity of symptoms persisted unabated. Of the remaining three patients one was better than during the previous season with phylactic injection therapy, one was better than during the previous season when no treatment was given and the result in the third is not reliable, for he reported "weakness" for forty-eight hours following a number of the saline injections and discontinued both the potassium chloride medications and the pollen injections. Of sixteen patients to whom phylactic and incomplete preseasonal pollen injections, as well as potassium chloride, were given, five continued to have hay fever throughout the season; four reported immediate definite relief (with a few severe days throughout the season) and five reported considerable relief with only moderate hay fever through the remaining part of the season. Of fifty control patients who received a complete series of standard pollen injections, twelve had five or more days of severe hay fever, nineteen had fewer than five severe days and the remaining nineteen had no severe days. Of twelve patients with allergic coryza, only three reported any definite relief of symptoms with the addition of potassium chloride to their routine treatment. These three also noted periods of exacerbation of symptoms when taking potassium chloride.

Journal of Immunology, Baltimore

38:333-412 (May) 1940

Anaphylaxis in Rabbit: The Symptom of Fall of Blood Pressure. M. Rocha e Silva, São Paulo, Brazil.—p. 333.

Effect of Age on Spread of Dye in Skin of Normal, Antigenically Stimulated and Tuberculous Guinea Pigs. R. Y. Gottschall and W. E. Bunney, Lansing, Mich.—p. 345.

Serum Cholesterol in Horses During Immunization with Pneumococci, Including a Note on Hypercholesterolemia of Infectious Anemia. S. Member, M. Bruger and M. R. Chassin, New York.—p. 355.

Improved Serologic Method for Determination of Precipitative Titers of Antiserums. P. R. Cannon and C. E. Marshall, Chicago.—p. 365.

Sulfanilamide in Experimental Infections with Streptococci from Scarlet Fever and Erysipelas. Helen Cook Newman, Chicago.—p. 377.

*Bactericidal Power of Blood from Patients and Normal Controls for Staphylococci. W. W. Spink and J. R. Paine, with assistance of Jean Jermsta, Minneapolis.—p. 383.

Practical Assay of Type III Antipneumococcus Rabbit Serum by Mouse-Protective Test. A. Holm and G. F. Leonard, New Brunswick, N. J.—p. 399.

Blood Groups and MN Types of Eskimos: II. (District of Julianehaab, West Greenland). V. Fabricius-Hansen, Copenhagen, Denmark.—p. 405.

Bactericidal Power of Blood for Staphylococci.—Spink and Paine studied the antibacterial immunity of twenty-five patients with various types of staphylococcal lesions. Bactericidal tests were done on the bloods of these patients at various intervals during the course of their illnesses and after they had recovered. The bloods of eighteen individuals free from any known infection were used as normal controls. Thirty-one strains of staphylococci were utilized in performing the bactericidal tests. Seventeen of these strains were isolated from the patients' lesions. A bacteremia was demonstrated in six of the twenty-five. Three individuals died as a result of their infections. The most common type of lesion was osteomyelitis. All but one of the strains produced a pigment and therefore were classified with the *Staphylococcus aureus* group. Coagulase production was demonstrated for all but two strains, and also all but two fermented mannitol. All the strains possessed hemolysin for rabbit erythrocytes. According to their activity on crystal violet agar, all except one strain gave positive results. With the exception of a few patients, little bactericidal power resided in the blood for homologous strains. This is more

apparent for the bloods of the normal controls. On the whole, no definite correlation could be shown to exist between the bactericidal power of the patients' bloods and their clinical course. However, in some instances the bloods of patients killed an appreciable number of homologous organisms. In comparison with the foregoing, the bloods of both the patients and the normal controls were capable of killing heterologous organisms more consistently. The information reemphasizes the lack of an appreciable degree of killing power by human blood for pathogenic staphylococci, even though small numbers of organisms were killed in some instances. The more consistent bactericidal power of blood for the heterologous strains of staphylococci than for the homologous organisms can be partly explained on the basis that some of the heterologous strains were nonpathogenic according to one or more of the biologic tests that were employed. Organisms that did not ferment mannitol or coagulate human plasma were usually killed in large numbers. Non-pathogenic strains of staphylococci were killed by the whole blood, whereas pathogenic strains resisted the bactericidal action.

Journal of Lab. and Clinical Medicine, St. Louis

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Electrocardiographic Changes Induced by Exercise in Diagnosis of Coronary Insufficiency. L. H. Sigler, Brooklyn.—p. 796.

*Hypertension and Obesity: Statistical and Clinical Study of 10,883 Individuals. S. C. Robinson, M. Brucer and J. Mass, Chicago.—p. 807.

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Cultural Diagnosis of Tuberculosis Using Bordet-Gengou and Löwenstein-Jensen Media. Lucy Mishulov and Sadie Reavin, New York.—p. 876.

The Ido Test for Syphilis. B. R. Powers, Knoxville, Tenn.—p. 883.

Concentration of Tubercle Bacilli from Spinal Fluid by Means of Chemical Flocculation and Lipoid Solvents. J. H. Hanks and H. A. Feldman, Washington, D. C.—p. 886.

Cellular Exudates of Bowel Discharges.—According to Bercovitz, studies on cellular exudates carried out during the last four years have established that, whenever pathologic changes take place in the intestinal mucosa, cells of various types will be found in the discharge. Conversely, when no cells are found no pathologic condition is present. The presence or absence of these cells can be determined by microscopic examination of the discharges. Observations were made on 1,123 patients, who reported their bowel function to be absolutely normal. The specimens examined consisted of the normally passed bowel evacuations and the diarrheal discharge following dosage with magnesium sulfate. Of the 2,158 specimens obtained, 1,960 were normal. Magnesium sulfate was given to 127 patients, who passed 198 watery stools. Only eleven specimens out of the entire total were positive for cells. These specimens were obtained from two patients 57 and 62 years of age. Further study of them has not been possible. The results indicate that cells do not occur in the intestinal discharges of normal individuals even though magnesium is given to produce a diarrheal movement. For comparison the intestinal contents from several different levels in the gastrointestinal tract taken during postmortem examinations of seven individuals, scrapings from the intestinal walls at the same locations and specimens of the intestinal contents from three locations in the colon and

from the terminal ileum from three dogs were examined and found entirely negative for cells. The conclusion is drawn that, if no pathologic condition exists, cells will not be found on microscopic examination of the intestinal discharges.

Hypertension and Obesity.—Robinson and his associates present the result of periodic physical examinations of 10,883 apparently healthy residents of an urban region. The relationship between weight and blood pressure of the individuals was determined. Weight alone was found to be a poor measure of obesity. Instead, a ponderal index—weight divided by height—was used as an index of relative overweight. With an increase in age there was an increase in weight. After the age of 30 this increase in weight is probably a pathologic process. With an increase in ponderal index toward obesity there was a step-like rise in both mean systolic and diastolic blood pressures in men and women. The modal systolic and diastolic pressures increased with an increase toward heavier weight though not as markedly as did the mean. The per cent actual to expected ratio shows that obese men have almost three times more systolic hypertension and almost four and one half times more diastolic hypertension than do underweight men. Obese women have six times more systolic and diastolic hypertension than do underweight women. Obese men have only one half as many low systolic and only five eighths as many low diastolic pressures as do underweight men. The corresponding figures for women are three eighths and one half respectively. In any hypertensive group overweight is proportionately more common than underweight, and, conversely, in any low pressure group underweight is more common than overweight. Among obese men high systolic pressures are two and one half times more common than low pressures, while high diastolic pressures are three times more common than low pressures, and for overweight women high systolic and diastolic pressures are three times higher than low systolic and diastolic pressures. Among underweight men there are two and one half times more low systolic pressures than high systolic pressures and three and one half times more low diastolic pressures than high diastolic pressures. Among underweight women there are almost four times more low systolic and diastolic pressures than high systolic and diastolic pressures. In every age group (except women more than 60 years of age) there is an increase in mean systolic and diastolic pressures with an increase in weight. Among the overweight less than 45 years of age there are more low pressures than high pressures. This decreases with succeeding decades so that at the age of 45 there is a complete reversal and thereafter there are more high than low pressures. In every age group overweight men and women more often have high than low pressures. Low pressures are more frequent than high pressures in the underweight in every age group (except women more than 60 years of age). Likewise hypertensive men and women are more often overweight than underweight, and those with low pressure are more often underweight than overweight. In general, obesity and hypertension are frequently associated, but the significance of this fact must be withheld until the influence of body build on obesity has been appraised.

Journal-Lancet, Minneapolis

60:195-252 (May) 1940

- Some Aspects of Mental Hygiene Program in Early Childhood. W. S. Langford, New York.—p. 195.
 Etiology and Management of Speech Disorders. B. Bryngelson, Minneapolis.—p. 199.
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 Epilepsy Research and Mining. W. G. Lennox, Boston.—p. 205.
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 Diagnosis and Treatment of Leukorrhea. E. Allen, Chicago.—p. 221.
 Modern Conceptions of Backache. H. W. Meyerding and G. A. Pollock, Rochester, Minn.—p. 225.
 Diagnosis and Treatment of Eye, Ear, Nose and Throat Conditions of Particular Interest to the General Practitioner. A. D. McCannel, Minn. N. D.—p. 232.

Journal of Nervous and Mental Disease, New York

91:697-840 (June) 1940

- Organization of Psychoanalytic Procedure in the Hospital. D. M. Bullard, Rockville, Md.—p. 697.
 Paraphysal Cysts of Third Ventricle. H. Zeitlin and B. W. Lichtenstein, Chicago.—p. 704.
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 Intracranial Spinal Lipomas: Report of Case, with Remarks on Their Problematic Origin and Unusual Pathologic Characteristics. G. Wilson, H. Bartle Jr. and J. S. Dean, Philadelphia.—p. 745.
 On Epilepsy. O. Marburg, New York.—p. 754.

Journal of Nutrition, Philadelphia

19:415-516 (May) 1940

- Composition of Some Common Foods with Respect to Carbohydrate Content. T. M. Carpenter, Boston.—p. 415.
 Combustion of Carbohydrates in Man After Ingestion of Common Foods. T. M. Carpenter, Boston.—p. 423.
 Choline Metabolism: IV. Relation of Age, Weight and Sex of Young Rats to Occurrence of Hemorrhagic Degeneration on Low Choline Diet. W. H. Griffith, St. Louis.—p. 437.
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 Effects of Simple Dietary Alterations on Retention of Positive and Negative Minerals by Children. Icie G. Macy, Frances Cope Hummel, Helen A. Hunscher, Marion L. Shepherd and Helen J. Souders, with assistance of Mary Bates Olson, Priscilla Bonner, J. Horton, Louise Emerson and A. Theresa Johnston, Detroit.—p. 461.
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 Protein Anabolism in Organs and Tissues of Pregnant Rats at Different Levels of Protein Consumption. L. J. Poo, W. Lew, D. D. Lee and T. Addis, San Francisco.—p. 505.

New England Journal of Medicine, Boston

222:865-900 (May 23) 1940

- New England, Neurosurgery and the Neurosurgeon. W. J. Mixer, Boston.—p. 865.
 Minor Causalgia: Hyperesthetic Neurovascular Syndrome. J. Homans, Boston.—p. 870.
 *Extreme Leukocytosis and Acute Hemolytic Anemia Associated with Administration of Sulfanilamide: Report of Case. H. M. Spence and G. M. Roberts, Dallas, Texas.—p. 874.
 Endocrines: Use of Testosterone. J. C. Aub, Boston.—p. 877.

Leukocytosis and Hemolytic Anemia with Sulfanilamide.—Spence and Roberts report a case of acute hemolytic anemia following administration of sulfanilamide and point out that this disorder is one of the most serious complications of this drug. It is characterized by a rapid fall in the erythrocyte count and hemoglobin during the first few days of sulfanilamide administration. The process is apparently a peripheral hemolysis due to an idiosyncrasy to the drug and is unrelated to the dosage, concentration of sulfanilamide in the blood or type of infection. The bone marrow shows evidence of hyperplasia. The acute hemolytic anemia is to be distinguished from the comparatively slight, slowly developing drop in hemoglobin that commonly occurs when sulfanilamide administration is prolonged for ten days or more. Harvey and Janeway first described the acute anemia, reporting three cases. Wood reported twenty-one cases occurring among 522 patients treated with sulfanilamide, an incidence of 4 per cent. That this figure is probably considerably higher than the average is indicated by the comparatively few reports in the literature and by the fact that no case of acute hemolytic anemia, other than the one here reported, has been encountered in more than 2,000 patients who received the drug at the authors' hospital. The extremely high leukocyte count in the reported case, in contradistinction to the granulocytopenia usually considered a hazard of sulfanilamide, prompted the authors to analyze several cases of acute hemolytic anemia reported in the literature. They gained the impression that the leukemoid picture is an exaggeration of leukocytosis in other cases. They

have no explanation of its mechanism beyond suggesting that it may have been a concomitant of the marked bone marrow stimulation and hyperplasia. The treatment of the acute anemia involves withdrawal of the drug, forcing of fluids and maximum transfusions of blood. The convalescence is rapid after the patient surmounts the hemolytic crisis.

South Carolina Medical Assn. Journal, Greenville

36:135-158 (May) 1940

- Influence of Bromides in Mental Diseases. J. T. Cuttino, Columbia.—p. 135.
Official Syrups as Vehicles. J. H. Hoch, Charleston.—p. 139.
Diagnostic Significance of Upper Abdominal Pain. J. W. Ratliffe, Anderson.—p. 141.

Southern Medical Journal, Birmingham, Ala.

33:559-672 (June) 1940

- *Carcinoma of Lung: Analysis of 195 Cases, with Special Note on Needle Puncture Biopsy. C. J. Tripoli, New Orleans, and L. F. Holland, Austin, Texas.—p. 559.
Importance of X-Ray Interpretation in Treatment of Pulmonary Suppuration. B. Blades, St. Louis.—p. 565.
Biologic Action of Radiant Energy. E. R. Whitmore, Washington, D. C.—p. 572.
Stones of Recumbency. H. E. Carlson and N. F. Ockerblad, Kansas City, Mo.—p. 582.
The Grading of Rectal Cancer. T. E. Smith, Dallas, Texas.—p. 593.
Electrically Lighted Anoscope with Detachable Handle. J. H. Dodson, Mobile, Ala.—p. 600.
*Measles Complicating Pregnancy: Report of Twenty-Four Cases with Three Instances of Congenital Measles. I. Dyer, Tablequah, Okla.—p. 601.
Cerebellar Abscess: Review of Cases. H. Wilkins, Oklahoma City.—p. 605.
Etiology of Nerve Deafness, with Particular Reference to Quinine. S. B. Forbes, Tampa, Fla.—p. 613.
Primary Cutaneous Gilchrist's Disease. J. L. Callaway and V. Moseley, Durham, N. C.—p. 622.
Studies in Obstetric Analgesia. D. M. Paton, Houston, Texas.—p. 626.
Serodiagnostic Tests for Syphilis as Performed in State Laboratories in 1938 and 1939: Report of the Committee on Evaluation of Serodiagnostic Tests for Syphilis. H. H. Hazen, T. Parran, J. F. Maboney, Washington, D. C.; A. H. Sanford, Rochester, Minn.; F. E. Seneair, Chicago; W. M. Simpson, Dayton, Ohio, and R. A. Vonderlehr, Washington, D. C.—p. 633.
Analysis of Periodic Physical Examinations for Five Years. J. J. Brandabur, Huntington, W. Va.—p. 638.
Treatment of Typhoid Fever by Thiazole Derivatives of Sulfanilamide: Preliminary Report of Four Cases. J. O. Weilbaecher Jr., Emma S. Moss, H. M. Taylor and H. Dupuy, New Orleans.—p. 645.
Some Medicolegal Aspects of Alcoholic Intoxication. F. C. Helwig, Kansas City, Mo.—p. 648.
Indications for and Results of Splenectomy. H. D. Collins, Oklahoma City.—p. 656.
Roentgenologic Bone Manifestations in Certain Generalized Diseases of Infants and Children. W. D. Anderson and J. G. Hughes, Memphis, Tenn.—p. 660.
Note on Effect of Alpha-Tocopherol (Vitamin E) in Human Nutrition. T. D. Spies, Birmingham, Ala., and R. W. Vilter, Cincinnati.—p. 663.

Carcinoma of Lung.—According to Tripoli and Holland, the advent of lobectomy and pneumectomy has entirely changed the outlook in many cases of carcinoma of the lung, a disease in which until recently the prognosis was hopeless. The question of what these methods can achieve depends entirely on prompt diagnosis. The authors present an analysis of 195 cases of primary carcinoma of the lung. Pulmonary carcinoma now represents 10 per cent of all malignant tumors, improved diagnostic methods having resulted in a marked increase in the frequency of recognition. The incidence in white patients is more than double that in the Negro, and the male incidence is seven times higher than the female. The largest number of cases occurs in the sixth decade of life. The etiology is unknown. The classification into reserve cell, columnar cell and squamous cell carcinoma is believed to be most reasonable. Chest pain, cough, hemoptysis, loss of weight, dyspnea, persistent expectoration and fever are the chief symptoms in the order of frequency. There are no notable physical signs, although atelectasis and pleural effusion are often present. Most physical signs are the result of the malignant process and not signs of the disease per se. Roentgenologic examination, bronchoscopy, bronchography and thoracoscopy are all useful diagnostic methods, though the latter has only a limited field. For the last year the authors have employed punch biopsy of superficially located tumors as a diagnostic method

and have repeatedly demonstrated its efficacy. They use a needle which operates on the principle of a trocar. It consists of a short hollow outer needle with a beveled edge containing a smaller-bore hollow needle. The inner needle is longer than the outer needle and is divided in the center. The cutting edge of the inner needle is beveled in the shape of a V. The technic consists of little more than the simple insertion of the two needles, one within the other, in the same manner in which an aspirating needle would be inserted. Local anesthesia is used, and a small incision is made in the skin before the needle is inserted both to facilitate its entrance through the chest wall and to eliminate the possibility of including skin in the biopsy specimen, which might lead to an incorrect diagnosis of squamous cell carcinoma. The proper selection of cases is the first principle of both safety and success. Tumors in the trachea, the bronchi or the primary bronchial subdivisions, which are readily accessible through a bronchoscope, should not be subjected to puncture through the chest wall. Punch biopsy is applicable only to tumors situated in the periphery of the lung near the pleural surface, and the site of puncture should be the point at which the lung tumor is most superficial, this location having been determined by the taking of roentgenograms in various positions.

Measles Complicating Pregnancy.—Dyer observed twenty-four cases of measles complicating pregnancy over a period of three months. These cases were discovered in the rural district included in the five county demonstration area in northeastern Oklahoma. The occurrence of a rather widespread epidemic over a five county area provided data which offer an opportunity to present comparative figures, some of which are at variance with the information thus far presented in the literature. In the present material the age of occurrence ranged between 14 and 42 years. Pregnancy was interrupted in 37.5 per cent, and 25 per cent of these were at or near term. Three babies exhibited measles at birth or two days later. A laparotrachelotomy was performed on one mother at the height of her exanthem because of a pelvic contraction and persistent labor. There was no maternal mortality, but the postpartum course of one woman was febrile. This was three weeks after the attack of measles. The author thinks that measles probably occurs more frequently during pregnancy than the literature of the last twenty years indicates. The effects on pregnancy were, however, not so serious as is indicated in the literature.

Southwestern Medicine, El Paso, Texas

24:149-184 (May) 1940

- Organized Medicine: A Professional Guild. D. F. Harbridge, Phoenix, Ariz.—p. 149.
Tube Decompression in Intestinal Obstruction. L. C. Bennett, Los Angeles.—p. 152.
Spinal Injuries with Nerve Damage. R. M. Stuck, Denver.—p. 157.
Treatment of Inflammatory Lesions by Radiation. D. von Briesen, El Paso, Texas.—p. 160.
*Treatment of Cancer of Breast by Combined Irradiation and Operation. L. Eloesser, San Francisco.—p. 162.
Extradiabetic Uses of Insulin. A. T. Goldberg and M. M. Schatz, Fresno, Calif.—p. 165.

Irradiation and Operation for Cancer of Breast.—Eloesser describes a method for treatment of mammary cancer which includes (1) preoperative irradiation of the breast, axilla and supraclavicular regions (from 600 to 900 roentgens to each area), (2) removal of the breast, dissection of the axilla with a Percy cautery and (3) intra-operative delivery of a heavy dose (from 2,500 to 3,000 roentgens) of unfiltered or lightly filtered x-rays to the open wound for cancers with probable axillary involvement. The ray is centered toward the areas that appear most suggestive. This treatment takes from twelve to eighteen minutes. The purpose of this heavy intra-operative irradiation is different to that of the mild preoperative course. Preoperative treatment is given with the idea of making the fields into which cancer cells may likely be scattered during operation unfit for their future growth. It is kept moderate so that the lymphoid defense will not be broken down and the patient upset. It is not prolonged, so that the operative area may not be scary and stiff and likely to break down later. The massive

dose delivered during operation is sufficient, in theory at any rate, to kill cancer cells traversed by it. Necrosis and sloughing are not to be feared, as fascia, muscle, nerves and vessels that fall into the field are resistant to x-ray necrosis; the skin is kept shielded and out of the way. Even though aseptic necrosis may occur in the deeper soft parts later, these are protected by normal skin from ulceration and sloughing. The absence of cutaneous recurrences or lenticular metastases even in patients whose cancers reached the corium has fully borne out Murphy's experiments on mice on the value of cutaneous irradiation as a protection against implants. Not only the skin but other areas of lymphatic tissue seem to have been protected by the pre-operative and intra-operative irradiation. The author states that there have been a few deviations from the foregoing plan, which has been constantly followed for twenty years.

Surgery, St. Louis

7:647-808 (May) 1940

- *Results of Gastro-Enterostomy in Gastric and Duodenal Ulcers: Report of 106 Cases Followed for an Average of 7.1 Years Postoperatively. R. E. Church and J. W. Hinton, New York.—p. 647.
- *Carcinoma of Gallbladder: Etiologic Role of Gallstones. R. Warren and F. G. Balch Jr., Boston.—p. 657.
- Choice of Operative Methods for Carcinoma of Rectum. F. W. Rankin, Lexington, Ky.—p. 667.
- Acute Nonmalignant Perforations of Colon. J. Koucky and W. C. Beck, Chicago.—p. 674.
- Treatment of Postoperative Abdominal Distention with Prostigmine. E. J. Gordon, New York.—p. 686.
- Effect of Colchicine on Human Carcinoma. L. Seed, D. P. Slaughter and L. R. Limarzi, Chicago.—p. 696.
- Cystometric Timing of Catheter Removal from Neurogenic Bladder. M. Muschat, Philadelphia.—p. 710.
- Study of Varicose Veins: Report of 600 Cases. S. Z. Hawkes and G. F. Hewson, Newark, N. J.—p. 714.
- Intracystic Papilloma of Breast. N. F. Hicken, Salt Lake City.—p. 724.
- Surgical Treatment of Roentgen and Radium Dermatitis. R. K. Ghormley and R. D. Fairchild, Rochester, Minn.—p. 737.
- Investigation of Traumatic Shock Bearing on Toxemia Theory. D. B. Kendrick Jr., H. E. Essex and H. F. Helmholtz Jr., Rochester, Minn.—p. 753.
- Ununited Fracture of Neck of Femur: Report of Fifty-Nine Consecutive Cases. P. B. Magnuson, Chicago.—p. 763.
- Anatomic and Roentgenologic Study of Wrist Joint: Observations on Case of Recurrent Radiocarpal Dislocation Complicating Madelung's Deformity and Its Surgical Correction. T. Horwitz, Philadelphia.—p. 773.
- Mallet or Baseball Finger. E. B. Kaplan, New York.—p. 784.

Gastro-Enterostomy in Gastric and Duodenal Ulcers.—Church and Hinton report the results of continuous follow-up of 106 cases of gastro-enterostomy for periods of at least one year and for an average of 7.1 years. The continuous follow-up was based on the belief that a single observation after a lapse of one or several years is quite misleading. The symptomatology of peptic ulcer is a cyclic phenomenon. Unless there are frequent periods of observation, this periodicity may be lost sight of. The authors tried to follow their patients at intervals of three months and to make x-ray examinations every six months. The 106 patients have been tabulated in three categories. In the group of the cured were placed all patients who have been symptom free since operation, have eaten regular food, have performed their customary duties and have resumed their normal positions in life. There were twenty-six (24.5 per cent) in this group. In the group of the benefited were included those persons who, although suffering from a mild recurrence of symptoms and mild digestive disturbances, were able to resume their former activities. These patients must observe dietary restrictions and supplement them by occasional medication. Thirty-one cases, or 29.2 per cent, belong to this group. The category of the unimproved included patients who received no relief or who actually became worse as well as those who experienced recurrences of symptoms with their original intensity. There were forty-nine patients (46.2 per cent) in this group. Twenty, or 18.8 per cent, of 106 patients were found by two or more x-ray examinations or by operation to have gastrojejunal ulcers. In these cases the average time before the ulcer was proved was 4.95 years. In six others (5.6 per cent) one x-ray examination and the symptomatology suggested gastrojejunal ulcer. In these the average time before the condition was suggested was three and one half years. Preoperative hemorrhage had occurred in fifteen of the 106 cases. Seven, or

almost 50 per cent, of these had postoperative hemorrhages, at an average of 4.43 years after operation. In ninety-one cases in which operation was performed in the absence of preoperative hemorrhage, postoperative hemorrhage occurred after a similar lapse of time in fifteen, or 16.5 per cent. The end results of gastro-enterostomy in cases of obstruction and acute perforation are illuminating; in 63 per cent of the obstruction group improvement resulted, while 27 per cent were unimproved or were made worse. The results obtained by the authors do not produce so favorable a view of gastro-enterostomy as is generally presented by other writers. They think that this is presumably due to the longer follow-up period.

Gallstones and Carcinoma of Gallbladder.—According to Warren and Balch, a numerical expression of the risk of developing carcinoma that a person with gallstones runs would be of great help in deciding on the proper form of treatment of a patient in whom stones have been discovered but in whom symptoms are minimal or absent. It was with this point in mind that the present study was undertaken. The sources of information have been the files of the Massachusetts General Hospital and the medical literature. Between January 1898 and June 1939 there were admitted to the hospital eighty-four cases of primary carcinoma of the gallbladder. All cases of carcinoma of the bile ducts were excluded from this series. Other statistics were gathered from 8,000 consecutive necropsies between 1896 and 1936, from 109,646 consecutive hospital admissions from January 1925 to June 1939, and from 1,528 operations for cholelithiasis from January 1925 to December 1936. The authors found that carcinoma of the gallbladder is not a frequent disease in their locality, occurring in the present series about one third as commonly as carcinoma of the pancreas. Although carcinoma of the gallbladder may occasionally develop in the absence of gallstones, the great majority of cases are associated with gallstones which precede the development of the tumor. The exact percentage of cases of gallstones in which carcinoma of the gallbladder develops is impossible to determine accurately but probably lies between 1 and 2.5. No clinical criteria have been established to tell in which cases of gallstones carcinoma of the gallbladder will develop. Although carcinoma of the gallbladder is practically incurable once the diagnosis is established clinically, the risk of carcinoma developing in any case of gallstones is so small as not to indicate prophylactic cholecystectomy for that reason alone. The decision as to the advisability of cholecystectomy in cases of gallstones with few or no symptoms should be governed by a consideration of the danger of nonmalignant complications rather than by the risk of carcinoma of the gallbladder.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

48:275-332 (May) 1940

- *Pneumonectomy for Bronchiogenic Carcinoma: Report of Five Cases with Operative Recovery in Four. P. C. Samson, Oakland, Calif., and E. F. Holman, San Francisco.—p. 275.
- Gross Physiologic Principles of Head Injury Treatment. H. v. Briesen, Los Angeles.—p. 284.
- *Sterilization Procedures on Women. E. M. Lazard, Los Angeles.—p. 294.
- Some Endocrine Factors Responsible for Sterility in Women. E. C. Hamblen, Durham, N. C.—p. 300.
- Endocrines and Calcium Metabolism. L. Gunther, Los Angeles.—p. 304.
- Abdominal Pregnancy at Term: Case Report. R. N. Hamblen, Spokane, Wash.—p. 310.
- Disturbance of Carbohydrate Metabolism in Hyperthyroidism. H. J. John, Cleveland.—p. 313.
- Fallacies of Delayed Treatment of Perforative Appendicitis. C. A. Bachhuber, Los Angeles.—p. 317.
- Zinc Salts: Eventual Therapeutic Resource in Utero-Ovarian Troubles. H. Vignes, Paris, France.—p. 320.
- Hyperparathyroidism—Normal Chemistry—Rapid Recalcification Following Removal of Large Parathyroid Adenoma. C. J. Baumgartner, Los Angeles.—p. 324.

Pneumonectomy for Bronchiogenic Carcinoma.—Samson and Holman report total pneumonectomy for pulmonary carcinoma of five patients with four postoperative recoveries. Two of these patients are well (seven months and one year), one died one year after the pneumonectomy from coronary thrombosis and one was well for four months, after which signs of probable cerebral metastasis appeared. There was no evidence of recurrence or metastasis in the patient who died. The

authors state that pneumonectomy should no longer be considered as heroic surgery but in competent hands as an accepted method of treatment. Only seven years has elapsed since the first successful operation, but all indications point to an increasing number of cures and a substantial reduction in the operative mortality. As to the relative merits of lobectomy and pneumonectomy, they feel that lobectomy should be mentioned only to be condemned. Even with peripheral neoplasms the necessary mass ligation used in lobectomy is inadequate and unsurgical. Total pneumonectomy is entirely analogous to radical resection for carcinoma elsewhere in the body. Preoperative preparation, anesthesia, operative technic and postoperative care are all equally important factors in a successful pneumonectomy. As with carcinoma elsewhere, relatively early diagnosis is paramount if surgery is to be effective. Bronchiogenic carcinoma should be always kept in mind when an unexplained and persistent cough or thoracic symptom complex is presented. When the textbook picture of carcinoma of the lung (great loss of weight, pain in the chest, pleural effusion, copious purulent sputum, blood streaking and hemoptysis) is present it is too late to do more than to make a diagnosis. The condition must be suspected earlier and adequate confirmation sought by x-ray examination, fluoroscopy, bronchoscopy and biopsy.

Sterilization Procedures on Women.—Lazard believes that the simplest and least dangerous of sterilization procedures on the tubes is the crushing and tying of a loop of each tube, the Madlener technic. However, failures have been reported with this as well as with all the other methods of tubal sterilization. Ectopic pregnancies have been reported following such sterilization, and such procedures carry a definite increase in mortality risks because of embolism and intestinal adhesion and obstruction. For elective sterilization at the time of cesarean section he has favored supracervical hysterectomy over any method of tubal sterilization. The main objections to hysterectomy are that it is technically more difficult and that it subjects the patient to a premature menopause. It is the surest and safest method of sterilization. There was no fatality in 106 consecutive cases of elective hysterectomy for sterilization. If there is no associated pathologic condition, it does not as a rule produce the menopause unless the patient is at or near the menopausal age, in which case the menopause is not caused by the hysterectomy but by the changes in the ovaries due to age. Removal of the body of the uterus eliminates the possibility of future pathologic changes, such as fibroids, malignant conditions of the body or uterine endometriosis. The patient and her husband should understand that this sterilization is permanent.

Yale Journal of Biology and Medicine, New Haven 12:451-604 (May) 1940

- Lesions of Larger Vessels Following Renal Artery Constriction. M. C. Winternitz and L. L. Waters, New Haven, Conn.—p. 451.
- Postoperative Management of the Neurosurgical Patient, with Particular Reference to Nursing Problems. O. Turner, New Haven, Conn.—p. 459.
- Differentiation Between Sarcomatous and Leukemic Lymphocytes in Mice. A. Kirschbaum, W. U. Gardner, R. Nahigian and L. C. Strong, New Haven, Conn.—p. 473.
- Electrometric Study of the Healing Wound in Man. H. S. Burr, M. Taffel and S. C. Harvey, New Haven, Conn.—p. 483.
- Immunization with Tetanus Toxoid: The Recall Response. H. B. Streng, New Haven, Conn.—p. 487.
- Renal Hypertrophy in Mice Receiving Estrogens and Androgens. C. A. Pfeiffer, V. M. Emmel and W. U. Gardner, New Haven, Conn.—p. 493.
- Study of Temperature and Electric Potentials in Menstrual Cycle. Dorothy Smith Barton, New Haven, Conn.—p. 503.
- Effect of Antituberculosis Serum on Development of Experimental Tuberculosis of Skin. R. M. Thomas and F. Duran-Reynals, New Haven, Conn.—p. 525.
- Effect of Ablation of Hypophysis on Weight of Kidney of Rat. M. McQueen-Williams and K. W. Thompson, New Haven, Conn.—p. 531.
- Strain-Limited Development of Tumors of Pituitary Gland in Mice Receiving Estrogens. W. U. Gardner and L. C. Strong, New Haven, Conn.—p. 543.
- Further Studies on Prophylaxis of Experimental Infections and Intoxications with Various Hormone Preparations. L. Weinstein, New Haven, Conn.—p. 549.
- Retardation of Mammary Involution in Mouse by Irritation of Nipples. C. W. Hooker and W. L. Williams, New Haven, Conn.—p. 559.
- Physiologic Significance of Choline Esterase. D. Nachmansohn, New Haven, Conn.—p. 565.
- Some Properties of Staphylococcus Culture Filtrates. G. H. Smith, New Haven, Conn.—p. 591.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Australian and New Zealand J. Surgery, Sydney 9:331-434 (April) 1940

- J. H. Webb and the Early History of Appendectomy. K. F. Russell.—p. 333.
- Deformities Affecting Lower Radial Epiphysis. D. J. Glissan.—p. 337.
- Colonic Drainage: Plea for Cecostomy. W. Maxwell.—p. 342.
- New Method of Performing Encephalography. F. F. Ellis.—p. 345.
- Thoracoplasty in Pulmonary Tuberculosis: General Survey of Forty-Seven Cases. A. M. Hutson.—p. 359.
- Recent Thoughts on Orthotics. J. B. Hamilton.—p. 378.
- Liver Damage in Thyrotoxicosis. N. Wyndham.—p. 385.
- Technic of Panhysterectomy. F. A. Maguire.—p. 393.

British Medical Journal, London 1:799-838 (May 18) 1940

- Concentrated Serum in Treatment of Traumatic and Histamine Shock in Experimental Animals. C. H. Best and D. Y. Solandt.—p. 799.
- Successful Chemotherapy for Hemolytic Streptococcus Meningitis and Pneumococcal Meningitis in the Same Patient. W. O. Reid and J. F. Lipscomb.—p. 802.
- Treatment of Pneumococcal Meningitis with Sulfapyridine. S. T. Falla.—p. 804.
- *Clinical Experience in Electrically Induced Convulsions. F. E. Fox.—p. 807.
- Axial Rotation of Pregnant Uterus. G. S. Adam.—p. 808.

Electrically Induced Convulsions.—Fox presents a clinical account of the results obtained by electrically induced convulsions in seven psychotic patients, because he thinks that it is only by consideration of individual case histories that patients suitable for this treatment can be selected. The histories indicate that several patients had schizophrenia; others had catatonic stupor, psychiatric anxiety, depressive stupor and agitated melancholia. The author classifies the results of the electrical convulsions according to the degree of remission achieved. He designates as class A a complete return to normality and social intercourse outside the mental hospital, as class B a marked improvement in behavior, as class C no change, the patient still requiring constant attention. He places four patients in class A and the other three in class B. The electrically induced convulsions have advantages over other forms of convulsion therapy. 1. The patient suffers no unpleasant memories. 2. The loss of consciousness is instantaneous. 3. The possibility of fracture seems to be remote, provided certain precautions are taken. 4. The patient is willing to cooperate after the first two or three shocks. 5. The treatment can be quickly and easily carried out. 6. The appetite is stimulated. 7. The chronic constipation associated with these types of psychosis disappears early in the treatment. 8. The apparatus is portable. 9. The manipulator need not be a highly qualified electrical technician. Although the ultimate prognosis of this form of treatment is problematic at the present time, there seems no reason why the remissions should not be prolonged indefinitely by "maintenance" shocks if the patient is found to be relapsing. The contraindications to shock treatment would seem to be arterial and cardiac diseases, high blood pressure and intracranial diseases.

Lancet, London

1:911-954 (May 18) 1940

- Blood Group Tests in Disputed Paternity: Report of Fifty Cases. D. Harley and G. R. Lynch.—p. 911.
- Death in the First Month and the First Year. C. McNeil.—p. 912.
- *Toxoid Treatment of Recurrent Infection After Staphylococcal Osteomyelitis. F. C. O. Valentine and E. C. B. Butler.—p. 914.
- Leukemic Lymphadenitis with Extensive Subcutaneous Deposits. Joab Bates and G. L. Haine.—p. 917.
- *Response of Nongravid Human Uterus to Posterior Pituitary Extract and Its Fractions Oxytocin and Vasopressin. A. McLellan.—p. 919.
- Intravenous Injection of Oxygen Under Normal Atmospheric Pressure. I. Singh and M. J. Shah.—p. 922.
- Rupture of Branch of Splenic Artery Associated with Pregnancy. D. MacLeod.—p. 924.

Toxoid in Recurrent Staphylococcal Osteomyelitis.—According to Valentine and Butler, recurrence of infection after osteomyelitis is rare, but thirty patients of this type were examined at the London Hospital in less than two years. Patients in whom repeated infection takes place at the site of

war wounds in which the bone has been injured may be placed in a similar category. The authors observed two patients in both of whom recurrence had been frequent and had latterly caused chronic ill health. Since one of them appeared to derive much benefit from injections of toxoid, the authors decided to investigate the degree of immunity prevailing in patients with recurrence and to study the effect of the treatment in cases in which recurrence had been frequent. The object was to maintain the level of immunity in order to lessen the tendency toward further attacks. Serologic investigations convinced them that the titers of antihemolysin do not suggest that much immunologic significance can be attached to this antibody but that it is at least possible that the general symptoms in staphylococcal infection are largely due to the alpha-hemolysin, for it has seemed to them that it is this factor rather than the leukocidin which is responsible for the reaction encountered in treatment with toxoid. Toxoid has therefore been prepared from toxins mixed to give a strong leukocidin and a moderate hemolysin. Beginning with 0.2 cc. of a 1 in 20 dilution the authors have used weekly injections until the patient could take the maintenance dose of 0.3 cc. of undiluted toxoid intramuscularly in the deltoid. This dose is then given at intervals of two or three months. The injections are continued for a period of years to maintain a high level of antitoxic immunity. Antitoxins in the serum of these patients are seldom high and often within normal limits. Antitoxins may reach higher levels in the pus than in the serum. The results suggest that a titer of about 0.32 K antileukocidin is usually required for the localization of infection in soft tissues. There has not yet been time to evaluate the treatment in preventing further recurrence. It is possible that occasionally the injections may stimulate activity in a new latent focus. The treatment is probably of value in cases with symptoms of persistent toxemia; e. g., war wounds.

Response of Nongravid Uterus to Solution of Posterior Pituitary.—McLellan recorded uterine contractions of forty-three women at various stages of the menstrual cycle. Sixty records were obtained. The women were all of reproductive age, 20 to 40, and thirty-four had borne children. Menstruation was regular at the time of observation. The movements of the uterus were recorded by introducing a small rubber bag filled with water into the uterus and by registering the changes in volume. The cervix was dilated to No. 6 Hegar. When the uterine movements had become more or less constant, graduated doses of the posterior pituitary fractions were administered intravenously. The reactivity of the uterus to solution of posterior pituitary and its fractions was determined by finding the minimal effective doses of these at various stages of the menstrual cycle. Twenty-eight of the sixty records showed that the uterus responded to solution of posterior pituitary or its fractions. The records comprising the responsive group were obtained immediately before or during menstruation and in the early interval part of the cycle; that is, the uterus responded to solution of posterior pituitary immediately before and during menstruation and in the early interval part of the cycle. The nongravid human uterus is caused to contract by vasopressin and not at all by oxytocin.

1:955-992 (May 25) 1940

Rational Approach to Research in Chemotherapy. P. Fildes.—p. 955.
Treatment of Fractures of Upper Third of Shaft of Femur. J. R. Armstrong.—p. 957.

Vitamins D₂ and D₃ and Dihydrocholesterol in Congenital Thyroid and Parathyroid Deficiency. H. P. Himsworth and M. Maizels.—p. 959.

*Potency of Vitamins D₂ and D₃ in Osteomalacia and Late Rickets. Dagmar Curjel Wilson.—p. 961.

*Protamine Zinc Insulin and Soluble Insulin: Interaction in Combined Doses. G. M. Wauchope.—p. 962.

Vitamins D₂ and D₃ for Osteomalacia and Rickets.—To test the antirachitic potency of vitamins D₂ and D₃ Wilson chose Indians living an outdoor life in the Kangra valley. Rickets and osteomalacia affect the inhabitants of both sexes at all ages. In assessing the value of treatment attention was paid to subjective symptoms, including pain in the lumbosacral region, pelvic girdle, legs, ribs, shoulder girdle and arms; flexor (carpedal) spasm was also taken into account. The patients were chiefly women from 20 to 40 years of age. Males also were included and the total range was from 6 to

70 years. Patients with osteomalacia or with late rickets of similar grades of severity were grouped in pairs. Pure vitamin D₂ was given to one of each pair and pure vitamin D₃ in the same dosage to the other. The deformity and pain before treatment and the improvement after treatment were assessed independently by members of the staff of the Canadian Mission Hospitals. The patients were examined weekly and the degree of improvement was classified as none, slight, definite, good or cured. One large dose of either vitamin was given once a week. The observations were made on thirteen pairs of patients with osteomalacia and two pairs with late rickets, and treatment was continued for three or four weeks. The dose given to both members of a pair was either 10,500 or 21,000 international units of vitamin D weekly. With a weekly single dose of 10,500 international units of either vitamin progress was extremely slow and the patients noticed little improvement in their symptoms after two such weekly doses, became restive and were unwilling to have further treatment. Improvement followed subsequent treatment with a weekly single dose of 21,000 international units. With vitamin D₂ the results were definite in six, good in four, cure in four and slight in one, and with vitamin D₃ they were definite in six, good in six and cure in three. Of the fifteen pairs of patients, five pairs were treated with 10,500 international units from the start and observed for two or three weeks before the dose was increased. Another group of four pairs received 21,000 international units from the start. The results indicate that there was no difference in the clinical effectiveness of the two forms of the vitamin. However, the results obtained in the five pairs treated with the minimal dose show vitamin D₂ as the more active in one case and vitamin D₃ as the more active in three cases, while the two vitamins were of equal activity in one case. No ill effects were observed. In comparison with the degree of cure previously effected in treating similar cases with approximately the same total vitamin dosage but administered daily as cod liver oil or as irradiated ergosterol, the use of the spaced large doses was considered to shorten the treatment by at least two weeks.

Protamine Zinc Insulin and Soluble Insulin.—Wauchope states that the total quantity of insulin can be still further reduced if the doses of ordinary or soluble insulin and protamine zinc insulin are given in separate injections, one immediately after the other, instead of being drawn into the same syringe and injected together. Seventeen hospital patients, women of more than middle age, who were being balanced on a combined dose of the two kinds of insulin, had blood sugar curve estimations on two different days: on the first day the protamine zinc insulin and soluble insulin were given in the same syringe and on the second day they were given separately. The two postinsulin blood sugar curves of these seventeen patients and those of five long standing cases of diabetes in full activity were plotted, one in each case being estimated after separate injections and the others after the two kinds of insulin had been mixed in the syringe. When the two insulins were drawn into the same syringe, the action of the ordinary insulin was modified. Some of it was delayed in action and some of it apparently lost. In all cases a larger proportion of soluble insulin was needed when given in the same syringe with protamine zinc insulin to produce a hypoglycemic action in the early part of the day. Therefore it seems that more economical and more accurate balancing is ensured when soluble insulin and protamine zinc insulin are given in separate injections. If drawn into one syringe they must not be allowed to mix. The hardened diabetic patient does not mind two pricks, and all who lead active lives prefer to take all their insulin in the morning rather than have to remember a second injection; hence the use of the two insulins is preferred by the patient and besides it ensures a more steady blood sugar level throughout the day and night.

Tubercle, London

21:185-216 (March) 1940

Mass Radiologic Examination of Chest. S. C. Shanks.—p. 185.
Technic Problems of Mass Radiography of Chest. P. G. Sutton.—p. 192.

Unsuitable Pneumothorax Treatment. S. Puder.—p. 197.

Annali dell'Istituto "Carlo Forlanini," Rome

4:157-300 (March-April) 1940. Partial Index

- *Pneumolysis (Jacobaeus' Operation) in Treatment of Hemoptysis. M. Morellini.—p. 157.
Lateral Diffusion of Pulmonary Tuberculosis in Elastic Anterolateral Thoracoplasty: Clinical and Pathogenic Study. M. Mario.—p. 193.

Pneumolysis in Tuberculous Hemoptysis.—According to Morellini, intrapleural pneumolysis (Jacobaeus' operation) is indicated in all cases of grave hemoptysis which occur in the presence of inadequate artificial pneumothorax and which cannot be controlled by increasing intrapleural pressure and by symptomatic treatment. The operation is performed under pleuroscopic control. When the adhesions cannot be completely resected, partial resection is done. The operation was successful in six grave cases reported by the author.

Atti d. Soc. Ital. di Ostetricia e Ginecologia, Rome

36:125-234 (March-April) 1940. Partial Index

- Lack of Coagulating Power in Blood of Maternal Placenta. F. D'Erchia.—p. 140.
*New Symptom of Renal Insufficiency in Albuminuria of Pregnancy. G. Piroli.—p. 142.

New Symptom in Albuminuria of Pregnancy.—Piroli observed the behavior of urea and nitrogen in the blood of ten pregnant women with albuminuria and in eight nonpregnant women with either liver disease or acute or chronic nephritis. Quantitative determinations of the blood were made three times with intervals of four hours in the course of one day and the determinations were repeated after an interval of several days. Patients were kept on water as the only drink during the days on which the determinations were made. Ambard's method was used. The women were between the seventh month of pregnancy and full term. Albuminuria with edema of the legs was pronounced in five cases and moderate and without evidence of edema in five. Azotemia remained unchanged in all patients in the last group, whereas it showed great oscillations in the blood of patients with grave albuminuria, as well as in the blood of the patients with liver and renal disease. The author found that moderate albuminuria may be controlled by either diet or medical therapy and that it disappears spontaneously after delivery. Grave albuminuria is more or less resistant to diet and medical therapy. It may diminish with either, or spontaneously after delivery, but in no case does it disappear entirely. The oscillations of ureo-azotemia in this group are independent of diet but are in proportion to the acuteness of albuminuria. The author concludes that changes of ureo-azotemia in albuminuria of pregnancy are an index of renal insufficiency and that variations within high figures show grave and probably irreversible renal lesions.

Gazzetta degli Ospedali e delle Cliniche, Milan

61:341-360 (April 28) 1940. Partial Index

- *Diffuse Muscular Metastases from Cancer of Sigmoid Flexure. A. Cattaneo and R. Storti.—p. 347.

Diffuse Muscular Metastases from Cancer.—According to Cattaneo and Storti, the development of multiple cancer metastases in striated muscles is rare. They report a case, in a man aged 29, of a primary adenocarcinoma of the sigmoid flexure which ran a rapid course and gave rise to diffuse metastases to the viscera, the skeletal bones and striated muscles. A diagnosis of true cancer metastases of the striated muscles was made by a biopsy. It was verified by a postmortem examination during which a small tumor was found at the sigmoid flexure which, on microscopic study, proved to be an adenocarcinoma.

Riforma Medica, Naples

56:465-500 (April 13) 1940. Partial Index

- *Diabetes as Cause of Diminishing Urinary Elimination of Hyperglycemic Substance. L. Antognetti and V. Patrono.—p. 467.
Physical Therapy of Poliomyelitis. G. Tullio Cataldo.—p. 475.

Diabetes and Hyperglycemic Substance.—Antognetti and Patrono stated in a previous communication that normal urine was found to contain a hyperglycemic substance. The present investigation concerns the urine of patients with diabetes mellitus and of a patient with hypophyseal adenoma, acromegaly and

insulin resistant diabetes. Extracts of individual specimens of urine were injected into rabbits and the glycemic reaction was determined. Injection of extract of urine of patients with diabetes mellitus caused hyperglycemia, which was higher than that caused by normal urine, whereas the injection of extract of urine of the acromegalic diabetic patient caused hypoglycemia. The authors express the opinion that the hypothetic substance is of hypophyseal origin, is diabetogenic and is related to hypoglycemic hypophyseal substances. Moderate hypophyseal dysfunction results in overproduction of hyperglycemic substances, which is a factor of importance in the pathogenesis of hyperglycemic diabetes. In the presence of a grave disturbance of the hypophyseal function and a severe anatomic lesion, hypoglycemic substances predominate and constitute the pathogenic factor of insulin resistant diabetes. Further researches along these lines are suggested.

Kinderärztliche Praxis, Leipzig

11:143-178 (May) 1940. Partial Index

- *Clinical Aspects and Therapy of Adiposal Gigantism. P. Laurentius.—p. 143.
Vitamin B₆ not Effective in Eczema of Nurslings. K. Schwartz.—p. 148.
Importance of Oxyuriasis and Treatment by Means of Resorcinol Derivative. H.-C. Hempel.—p. 149.
*Symptomatic Treatment of Serum Collapse. P. von Kiss and I. Flesch.—p. 155.
Two Attacks of "Generalized" Stomatitis Aphthosa of Unusual Severity. A. Windorfer.—p. 160.
Suggestions for Treatment of Weakness of Feet During Early Childhood. B. Roether.—p. 164.

Clinical Aspects and Therapy of Adiposal Gigantism.—Laurentius discusses adiposal gigantism, a temporary obesity of the puberal age which is frequently mistaken for disorders with a similar symptomatology but an entirely different pathogenesis. Thirty-four cases are reported. The history revealed, as a rule, that the obesity began at the age of 9 or 10 years. With the exception of seven cases, the food intake was not excessive; in ten cases the parents regarded it as deficient. The sudden increase in weight set in, in a few instances, after a severe or prolonged illness. The general complaints of these children are usually slight. Occasionally they complain of fatigue and of being unable to fulfil the requirements in gymnastics and in sports. The clinical examination discloses an excess of fat particularly on the chest, abdomen, hips and thighs. The excess in weight of these children, who vary in age between 9 and 14 years, amounts to from 5 to 26 Kg. (average 14 Kg.). The height is on the average 12 cm. above normal. The bony structure is surprisingly large and strong. This form of obesity is usually accompanied by a seemingly deficient sexual development. Follow-up examinations, however, disclosed that the hypogenitalism is apparent rather than real. The smallness of the penis may be simulated by the excess of adipose tissue. The circulatory organs are as a rule not impaired, and metabolic studies corroborated Niederwieser's observation that the basal metabolic rate is important only in cases of thyrogenic obesity. X-ray examination of the sella turcica and inspection of the fundus oculi give negative results. There is no agreement as to the etiology of adiposal gigantism, but it is suggested that a temporary dysfunction or hypofunction of the thyroid, the hypophysis and the gonads plays a part. The disorder may be mistaken for adiposogenital dystrophy (Fröhlich's syndrome). Differentiation here is important in the interest of a correct prognosis, which is favorable in adiposal gigantism but not favorable in adiposogenital dystrophy. Adiposal gigantism differs from the purely exogenous type of obesity in that the growth in length is not abnormal in the latter. A differential diagnosis is likewise important in the therapy of adiposal gigantism. A restriction of calories is tried and, if the decrease in weight is inadequate, endocrine treatment is begun by administering thyroid, gonadal and anterior pituitary extracts.

Symptomatic Treatment of Serum Collapse.—Von Kiss and Flesch observed severe circulatory disturbances in eleven patients who had received heterologous serum. Seven were less than 15 years old. The diagnosis is not difficult, because the collapse is usually preceded by the other symptoms of serum disease. Differentiation from diphtherial disturbances of the heart is possible not only on the basis of the difference in the

clinical picture but also on the basis of electrocardiographic examinations and of serial blood pressure controls. In diphtherial heart disease the blood pressure decreases gradually in the course of days, but in serum collapse it decreases rapidly almost from hour to hour. The electrocardiogram is definitely pathologic in diphtherial heart disease but not in serum collapse. Clinical observation, blood pressure determinations and electrocardiographic examinations must be continued during the treatment. At the onset of serum disease, ephedrine is given by mouth and the patient is kept in bed. If the systolic blood pressure falls to 80 mm. of mercury, epinephrine is injected at once even if there is no collapse. If pressure sinks so rapidly that collapse results before this intervention can be made, 0.1 cc. of a 1:1,000 solution of epinephrine mixed with from 10 to 20 cc. of a 20 per cent solution of dextrose is injected intravenously, and from 0.3 to 0.5 cc. of the epinephrine solution is at the same time injected into a muscle. In extremely severe cases one collapse may follow another almost hourly and the repeated insufficiency of the peripheral circulation may become complicated by a secondary cardiac failure. The cutaneous edema caused by the serum exanthem may make intravenous injections technically impossible; if this is the case a large vein must be surgically exposed, a cannula tied in and intravenous drip infusion continued for from twenty-four to twenty-eight hours. The drip fluid consists of physiologic solution of sodium chloride and 5 per cent dextrose. Necessary medicaments may be added to the fluid.

Klinische Wochenschrift, Berlin

19:241-264 (March 16) 1940. Partial Index

- Dysentery Among Troops in Polish Campaign. H. Otto.—p. 241.
Cardiac Lesions Due to Heat Stroke as Revealed in Electrocardiograms. E. Metz.—p. 247.
Therapeutic Effect of Dried Thyroid Gland Extracts in Goiter. E. Vertán.—p. 250.
*Endocrine Therapy in Hypertrophy of Prostate: Case. F. Bühler.—p. 254.
Vitamin C Deficiency in Exclusive Meat Diet. H. Rietschel.—p. 256.

Testosterone Propionate in Hypertrophy of Prostate.

—According to Bühler, testosterone propionate in massive doses promptly administered alleviates difficulties in urinating and associated distress even in advanced hypertrophy of the prostate. A man aged 72 had suffered from anuria for three days and the residual urine amounted to 1,500 cc. After twelve days of a daily dose of 25 mg., urination set in spontaneously. Three weeks later, dosage having been discontinued after the nineteenth day, the residual urine was reduced to 75 cc. No relapse had been reported as late as three and one half months. This patient was given a total of 475 mg. The author employs daily doses of 25 mg. until improvement occurs, thereupon reducing the quantity to 10 mg. Massive doses are required especially in grave cases belonging to the second and third stage of hypertrophic condition. The therapy is most effective in incipient and second stage prostate enlargement; in advanced cases in which surgical intervention is contraindicated because of the age of the patient or other complications, testosterone gives relief from pain. The author believes that the drug has prophylactic value if applied at the first signs of prostatic enlargement and that the study of constitutional types and a classification of their characteristics might indicate those in whom a predisposition to hypertrophy of the prostate exists.

19:337-360 (April 13) 1940

- *Active Protective Vaccination Against Bacillary Dysentery. R. Prigge.—p. 337.
Vitamin A Content of Some Vegetable Oils: Remarks on Report of Maxim and Bors.—p. 342.
Estimation of Conduction Time in Electrocardiogram. P. Scheer and D. Albers.—p. 343.
Sympathetic Nervous System and Vitamin A Exchange. W. Thiele and P. Guzinski.—p. 345.
Studies on Differing Insulin Sensitivity of Diabetic Patients. D. Decaneas and K. Uiberrak.—p. 347.
Investigations on Calcium Content of Normal Skin Compared with Aspects of Scleroderma. H. Kaether and K. W. P. Schaefer.—p. 353.

Vaccination Against Bacillary Dysentery.—According to Prigge the efforts to obtain a practical method of vaccination against bacillary dysentery have advanced chiefly along two routes: to produce a local immunity of the intestinal wall by

the oral administration of killed dysentery bacilli or to confer an effective protection by the parental, particularly the subcutaneous, administration of the entire body substance or of certain cellular constituents of the dysentery bacilli. It is now generally accepted that the Shiga-Kruse bacillus produces not only a toxin but also an endotoxin. The so-called toxin-deficient dysentery bacilli (Flexner, Kruse-Sonne and Schmitz bacilli) differ from the Shiga-Kruse bacilli in that they produce only an endotoxin (Schmitz bacilli produce small quantities of toxin in addition to the endotoxin). The endotoxins of the three "toxin-deficient" dysentery bacilli are readily differentiable from the endotoxin of the Shiga-Kruse bacillus. The protective immunization against the "toxin-deficient" dysentery bacilli has already been solved in its fundamental aspects. A polyvalent Flexner vaccine consisting of killed organisms was used with success in 1917. Effective protection against Shiga-Kruse dysentery is much more difficult and can be expected only if the vaccines contain both antigens, the endotoxin as well as the toxin, and if they contain large quantities of antigen which must be introduced into the organism in a suitable combination in order to avoid toxic actions. The author describes experiments with so-called ETA vaccines which contain endotoxin and toxin in combination with a specific antiserum or a nonspecific adsorbent. He found that the vaccines prepared according to the ETA principle produce in animals as well as in human subjects an immunizing alteration against the toxins of dysentery bacilli (Shiga-Kruse). Vaccinated animals tolerate an amount of toxin that is equivalent to twice the fatal dose in nonvaccinated animals. Serologic tests on human subjects disclose that after vaccination specific protective substances appear in the blood. The vaccines can be prepared in such a way that the reactions resulting from their administration are kept within tolerable limits. A final estimate of the efficacy of the ETA vaccines will be possible only on the basis of extensive clinical experience. If vaccination against dysentery is to be put into practice, polyvalent mixed vaccines must be employed which, in addition to the antigens of the Shiga-Kruse bacillus, contain also those of the most important "toxin-deficient" dysentery bacilli, Flexner and Kruse-Sonne.

Münchener medizinische Wochenschrift, Munich

87:501-524 (May 10) 1940. Partial Index

- Amputation and Increase in Blood Pressure. A. Bommes.—p. 501.
Experiences with Foot Amputation According to Pirogoff. K. Guth.—p. 502.
Vaccination Against Bacillary Dysentery. R. Prigge.—p. 503.
Peculiar Course of Chronic Osteomyelitis of Isolated Thoracic Vertebra. F. Schulz.—p. 507.
Changes in Conceptions of Causes of Diseases. E. Krueger.—p. 508.
*Electrical Convulsions in Psychiatry. A. von Braunmühl.—p. 511.
Loss of Therapeutic Action of Quartz Lamps with Age. E. Hasché.—p. 514.

Electrical Convulsions in Psychiatry.—Von Braunmühl directs attention to electrically induced convulsions, a method introduced by Cerletti and Bini and subsequently employed by Sogliani and other investigators. The correctly dosed electrical convulsion is characterized by immediate loss of consciousness and instantaneous onset of convulsions. The immediate loss of consciousness prevents unpleasant sensations. The electrically induced convulsions greatly resemble the metrazol convulsions. Whereas chemical convulsive agents exert a gradual and indirect stimulus on the parenchyma of the brain, the electrical method has an instantaneous and direct effect. This is clearly indicated by the convulsive reactions of the muscle groups of the lower extremities (jumping-jack movements). The apneic stage of electrical convulsion is short and respiration is quickly restored. Nausea or vomiting has not been observed. Surgical complications, such as dislocations of the jaw and compression fractures of the vertebrae, have been reported. Proper placement of the patient is therefore of great significance. A distinct advantage of the electrical convulsion therapy is that the veins do not have to be touched. These advantages and the fact that its effects are not inferior to those of chemically produced convulsions make the electrical method the therapy of choice. The electrical convulsion therapy is valuable in testing responsiveness in the old cases of schizophrenia and in the cases with a phasic course

in which relapses are likely. The author thinks that it might be possible to prevent the relapses by giving a short series of convulsions at intervals of one or two years. Such prophylactic application of electric shock is justified, since experiences heretofore have proved it harmless.

Zeitschrift für klinische Medizin, Berlin

137:243-364 (Feb. 26) 1940. Partial Index

- *Pathogenesis, Clinical Aspects and Therapy of Serum Sickness in Diphtheria. H. Hertel.—p. 243.
- Transient Pulmonary Infiltrations With and Without Eosinophilia of Blood. H. Löhr.—p. 297.
- Clinical Evaluation of Atrophic Cirrhosis of Liver Proved at Necropsy. R. Schubert.—p. 328.
- *Massive Doses of Eupaverine (a Morphine Derivative) in Embolism, Angina Pectoris and Bronchial Asthma. O. Dopffel and H. Kutschera-Aichbergen.—p. 341.
- Spectrography of Gastric Juice in Poisoning. J. Várady.—p. 354.

Serum Sickness in Diphtheria.—Hertel reports the drastic decrease (from a preceding average of 17.4 per cent to one of 3.7 per cent) in serum sickness complicating diphtheria observed during the course of nine and a half years and coincident with the adoption of a combined intravenous and intramuscular injection procedure, supported by a regimen of fruit and vegetable juices and daily enemas. The study was confined to 1,095 consecutive cases of diphtheria exhibiting 135 instances of serum sickness, three fourths of which occurred in children under 14 years of age. The greatest incidence of serum sickness was observed during the months of January, February and March. It was treated by slowly administering intravenously from 2 to 3 cc. of serum solution (from 2,000 to 3,000 international units) followed by intramuscular injections. The treatments were seconded by a complete withdrawal of the usual food, replaced by abundant juices. Twice daily enemas medicated with glycerin were administered. Istizin was given as a laxative. Subjective symptoms such as pruritus usually disappeared within twenty-four hours. Treatments were continued for three days after the cutaneous manifestations had disappeared, a vegetable and fruit diet bridging over the next two days before normal food ingestion was resumed. Recurrence following the violation of dietary directions promptly yielded with a return to the regimen. The author attributes the success of the therapy to the two phase injection plan, to vitamin C replenishment by vegetable and fruit juices of the seasonally impoverished system and to detoxication through intestinal washing out of bacteria. The increasing incidence of serum sickness with age may confirm bacterial implications. He believes that the therapeutic aids usually employed for controlling serum sickness involve needless distress to the patient and should be replaced by a more physiologic regimen.

Morphine Derivative in Massive Doses.—Dopffel and Kutschera-Aichbergen report excellent results obtained by massive doses of eupaverine, a morphine derivative, in embolism, angina pectoris and bronchial asthma. Primarily employed in large doses as a last recourse in desperate cases, the drug was observed to be well tolerated, to give unexpected relief and to be productive of significant improvements. Single doses ranged from 0.12 to 0.3 Gm., with the total daily dosage as high as 2 Gm. The drug was slowly administered, usually by the intravenous route, though intra-arterial injection is also indicated. In one case, in a person aged 46, of aortal embolism complicated by diabetes and arteriosclerosis in which gangrene had occurred in the right toe with extension over the dorsum of the foot, eupaverine obviated surgical intervention. The large ulcer on the foot not only healed but the toe was saved. A patient aged 74 with a badly damaged cardiac muscle was given 1.82 Gm. of the drug; not only was the pain eased but an improvement of cardiac action was noted. In a case of bronchial asthma in which the patient, aged 40, had been treated unsuccessfully for twenty years and in which dyspnea spasms would last for hours, suggesting imminent suffocation, eupaverine would restore normal breathing within a few minutes, though it left the disease unmodified. Total dosage in this case amounted to 7.68 Gm. The authors believe that eupaverine in large doses is the best remedy for angina pectoris and that serious attacks of bronchial asthma can be promptly checked by this drug. It is contra-indicated in pulmonary emphysema with cardiac lesions.

Vrachebnoe Delo, Kharkov

22:81-160 (No. 2) 1940. Partial Index

- *Tumors of Upper Thoracic Aperture. V. Melnikov and G. L. Derman.—p. 85.
- *Xiphoid Phenomenon and Its Diagnostic Value. M. M. Lyakhovitskiy.—p. 93.
- Anesthesia for Cesarean Section. A. M. Olshanetskiy.—p. 97.
- Treatment of Fermentation Enterocolitis and Suppurative Enterocolitis. A. V. Pines.—p. 99.
- Permissibility of Ligation of Appendix. Ya. L. Levi.—p. 103.

Tumors of Upper Thoracic Aperture.—Melnikov and Derman describe three cases of malignant neoplasm of the upper thoracic aperture. In their opinion the syndrome of Pancoast must be differentiated from the neoplasm of Pancoast, the latter being limited to a growth of branchiogenic origin arising from tissue above the dome of the pleura, whereas the former may be caused by a variety of tumors. The Pancoast syndrome includes a triad of symptoms caused by (1) symptoms of pressure on the brachial plexus, (2) symptoms due to pressure on the sympathetic trunk (Horner's syndrome) and (3) symptoms due to invasion of the ribs. The complete Pancoast syndrome is observed in (a) branchial cleft cancer, (b) bronchogenic cancer derived from the apex of the lung, (c) sympathicoblastomas and (d) supraclavicular fossa lymph node metastases. The Pancoast tumor is a definite and separate entity. It is branchiogenic in origin, does not invade the pleura or the apical lung tissue, invades and destroys the ribs, extends into the tissue of the neck and is particularly malignant. It is differentiated from tumors of the lung apex by the absence of cough and expectoration. The genesis of the Pancoast tumor is not clear. It may develop from the rests of the fourth and fifth branchial clefts, from aberrant lung tissue or from lateral aberrant thyroid. Some of these tumors may develop primarily in a rib from displaced embryonal cleft epithelium. Operative intervention in supra-pleural branchioma of Pancoast is possible in the earliest stages only. Irradiation is without effect. The intractable pain is best treated by a chordotomy or by section of the corresponding sensory roots.

Diagnostic Value of the Xiphoid Sign.—The incidence and the diagnostic value of the xiphoid sign has been observed, according to Lyakhovitskiy, in their clinic for the last ten years. Observations were made on 600 patients presenting disease of the gallbladder and the bile ducts, gastroduodenal ulcer, cancer of the stomach, the esophagus and the colon and acute abdominal emergencies. The clinical observations were verified at operation in the great majority of cases. The xiphoid sign consists in the presence of maximum tenderness at the tip of the xiphoid process, particularly on upward pressure. This sign was always present in the disease of the gallbladder or the bile ducts. Anatomic studies carried out in their clinic point to a direct lymphogenous as well as indirect lymph node connection between the gallbladder and the group of lymph nodes situated behind the xiphoid process. The author believes that acute lymphangitis and lymphadenitis just posterior to the xiphoid is the cause of the tenderness. He considers this tenderness to be a pathognomonic sign of cholecystitis and cholelithiasis.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

84:1385-1476 (April 13) 1940

- Renal Caruncle. L. D. Eerland.—p. 1386.
- Determination of Vitamin C Content in Blood and Urine of Patients with Cutaneous and Venereal Diseases. R. Kooij.—p. 1394.
- *Ulcerative Colitis Considered from the Surgical Point of View. A. Welcker.—p. 1400.
- Ureteral Fistulas: Reimplantation of Ureter into Bladder. C. van Staveren.—p. 1408.
- Polynueritis After Use of Uliron (Dimethyl-Disulfanilamide). S. J. R. de Monchy.—p. 1413.
- Schizophrenia and Criminality. S. P. T. Bakker.—p. 1416.
- Funicular Myelosis as Complication of Diabetes Mellitus. F. E. P. Meyjes.—p. 1420.

Ulcerative Colitis from the Surgical Point of View.—Patients with ulcerative colitis come to the surgeon, Welcker states, after having undergone treatment with diets, medicines, enemas, blood transfusions and bed rest and are often in a deplorable condition. Rectoscopy discloses severe inflammation, diffuse redness of the mucous membrane with small ulcers and considerable discharge of blood and mucus. Rectoscopy must be carefully prepared for, so that the view will not be obscured

by thin discharges, mucus, blood and pus. X-ray examination with contrast enema is of great diagnostic value, the picture being characterized by the so-called stove-pipe colon from which the normal haustra have disappeared. The course, complications and the treatment are discussed on the basis of nineteen cases observed. The author advocates colonic lavage by means of an appendicostomy or a cecal fistula. This treatment has the advantage that it can be carried out by patients themselves without interfering with their working capacity. In almost 75 per cent a good result was obtained and the opening could eventually be closed. If the regular and prolonged application of the lavage treatment does not produce the desired result, more radical methods may be considered, such as total exclusion of smaller or larger portions of the colon by an artificial anus. This treatment eventually leads to the removal of portions of the colon or rectum and has the disadvantage that the patients are unable to work for a long time.

84:1477-1588 (April 20) 1940

- Bleeding During Pregnancy. J. L. B. Engelhard.—p. 1481.
Congenital Arteriovenous Fistulas. P. Formijne.—p. 1487.
Case of Pneumococcal Meningitis After Acute Otitis Media, Cured by Operation of Ramadier, Sulfapyridine and Antipneumococcus Serum. P. G. Gerlings and C. M. Kröger-Wibaut.—p. 1494.
*Observations Regarding Significance of Erythema Nodosum for Epidemiology of Tuberculosis. P. Brouwer.—p. 1501.
Diagnosis and Treatment of Scabies. E. Zurbelle.—p. 1509.
Polyneuritis as Result of Gold Poisoning. E. Hoelen.—p. 1514.

Erythema Nodosum and Epidemiology of Tuberculosis.—Brouwer selected from among a hundred patients with erythema nodosum observed by him during the years 1936-1939 a number who had a source of tuberculous infection in their environment. A group of four contacts of a patient with infectious pulmonary tuberculosis presented symptoms within a comparatively short time; three had erythema nodosum and two of these simultaneously presented pulmonary changes which were interpreted as primary pulmonary tuberculosis. In another group, five children of a woman with infectious pulmonary tuberculosis presented signs of tuberculous infection. Two of the five still showed signs of erythema nodosum and in a third the history disclosed an earlier attack of erythema. The author presents five groups which emphasize the importance of erythema nodosum as a frequently observed symptom of a usually new tuberculous infection and its importance in the campaign against tuberculosis.

84:1589-1680 (April 27) 1940

- Outbreak of Attack of Glaucoma. G. F. Rochat.—p. 1597.
Sulfapyridine in Therapy of Epidemic Cerebrospinal Meningitis. W. A. Kuonen and A. J. C. Haek.—p. 1602.
Sulfapyridine in Meningococcal and Pneumococcal Meningitis. M. Weersma.—p. 1610.
Sulfapyridine in Throat, Nose and Ear Disorders. P. G. Gerlings.—p. 1616.
*Granulocytopenia in Two Sisters. N. Samsom.—p. 1623.
Oxyuris and Appendicitis. J. Schwarz and M. Straub.—p. 1627.
Several Peculiarities in "Normal" Electrocardiogram. R. van Wesel.—p. 1635.
Cure of Meningococcal Sepsis with Large Doses of Sulfanilamide. J. C. J. Burkens.—p. 1639.

Granulocytopenia in Sisters.—Samsom quotes the clinical history of a girl aged 16 who had chills, coughed and complained of pain in the left side. Treatment with sulfapyridine was instituted because pneumonia was feared. After a temporary improvement, a scarlatina-like rash was observed and this was followed three days later, when the patient was hospitalized, by severe dyspnea and cyanosis. Repeated blood examinations disclosed a rapid decrease in leukocytes. Injections of pentnucleotide, blood transfusions and other measures were without avail and the girl died. Inquiry into the family history disclosed that several years before a sister of the girl had died at about the same age as the result of granulocytopenia. Sulfapyridine had not been in use at the time of her death. It could not be determined whether she had received other medicaments that have been known to be followed by granulocytopenia such as aminopyrine, neo-arsphenamine, gold preparations or dinitrophenol. The question of a familial predisposition presents itself. It is generally believed that hypersensitivity to certain drugs is one of the most frequent causes of granulocytopenia and familial predisposition may play a part in this hypersensitivity. The author cites reports from the literature which corroborate this suggestion.

Nordisk Medicin, Gothenburg

6:711-778 (April 13) 1940

Medicinsk Revue

- *Epiphysiolysis of Head of Femur and Its Treatment. N. A. Nicolaysen.—p. 733.

Epiphysiolysis of Head of Femur and Its Treatment.—Nicolaysen reports nine cases of epiphysiolysis of the head of the femur treated by closed reduction and immobilization in plaster of paris in the Whitman position and nine treated by more conservative methods. He followed up all but one of these from one and a half to nine years. The end results were judged (1) from the subjective point of view, (2) clinically on the basis of shortening, muscular atrophy and motility according to the Ferguson and Howorth index and (3) anatomically from roentgenograms. In thirteen cases (more than 70 per cent) the results were good to excellent, in three good, and in two fair. The results of closed reduction were in every respect superior to those of conservative methods.

6:811-854 (April 27) 1940. Partial Index

Hygiea

- Experiences as Volunteer Civil Surgeon in Finland. J. Olow.—p. 833.
*Sternal Puncture and Its Practical and Theoretical Significance. N. G. Nordenson.—p. 834.

Sternal Puncture and Its Significance.—Nordenson states that from the diagnostic point of view bone marrow puncture has relative limitations. In vague anemias with sufficiently low red blood corpuscle values the diagnosis can be made by sternal puncture. Hyperplastic but normally normoblastic erythropoiesis usually occurs in pernicious anemia in remission, in essential hypochromic anemia, in hemolytic jaundice and in "erythroblastosis" in children. Hyperplastic erythropoiesis also appears in anemia due to hemorrhage, toxic anemia and anemia due to digestive disorders. Strongly degenerative myelopoiesis is pathognomonic for pernicious anemia and diagnosis can be made even if promegaloblasts and megaloblasts are few. In leukopenic myeloses and leukopenic lymphadenoses with vague peripheral blood picture the sternal punctate is typical and diagnosis is possible at an early stage. Lymphatic metaplasia of the bone marrow is pathognomonic for lymphadenosis. Sternal puncture is of great value in the differential diagnosis between lymphatic leukemia and infectious mononucleosis. In mononucleosis lymphatic bone marrow is absent and the bone marrow picture is largely normal. A hyperplastic megakaryocyte system often occurs in genuine polyglobulism and eventually in essential thrombocytopenia. The diagnosis of reticular and monocytic leukemia can be made during life by sternal puncture. In these diseases the bone marrow reticulum is strongly hyperplastic. In myeloma the bone marrow pictures show hyperplasia of the plasma cell types of the reticular cells. In vague febrile diseases which cause cachexia, sternal puncture is indicated. The diagnosis of Gaucher's disease can be made directly on the finding of typical Gaucher cells. The occurrence of cancer metastases is as a rule a surprise. Demonstration of protozoa and bacteria is of less interest. The effect of roentgen treatment can be seen in the bone marrow and the effect of extirpation of the spleen in hemolytic jaundice can be studied. Study of the origin of the blood cells by sternal puncture is superior to the pathologic-anatomic method. The reticular cell of the bone marrow is the mother cell of all cells. The "blast" cells are merely transition forms. The first marrow cells in the fetus consist of the primitive lymphoid reticular cells. In normal marrow this primitive cell functions as the mother cell of erythrocytes and plasma cells. In myelopoiesis the myeloblast functions as the mother cell, but in normal bone marrow certain transition forms from reticular cells to myeloblasts are absent. These forms are, however, seen in pathologic myelopoiesis, especially in myeloblast leukemia. The preliminary stages of thrombocytes and megakaryocytes are formed from the myeloblasts. In lymphatic metaplasia of the bone marrow direct transition forms from reticular cells to immature lymphocytes are seen, particularly in acute lymphoid leukemias. The origin of the monocytes continues uncertain but they apparently develop via the monoblasts from the reticular cells.

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SURGICAL NEUROLOGY AND BIOLOGY

CHAIRMAN'S ADDRESS

PAUL C. BUCY, M.D.

CHICAGO

I think my description of the mode of operating and of the anatomy of the part concerned, clear enough to enable any good anatomist, possessing the judgements requisite for a surgeon, to operate with safety. I hope no operator of any other description may even attempt it. It is my most ardent wish that this operation may remain, to the mechanical surgeon, forever incomprehensible. Such have been the bane of the science; intruding themselves into the ranks of the profession, with no other qualification but boldness in undertaking, ignorance of their responsibility and indifference to the lives of their patients. —*Ephraim McDowell*, 1819.

Although cranial surgery was undoubtedly practiced by prehistoric man and by his descendants, little progress was made, and this type of surgery, apart from the relief of demons in individuals suffering from epilepsy and psychoses, was confined to the treatment of wounds and fractures and of other externally visible conditions until the last quarter of the last century. At that time a renaissance of interest in the nervous system was initiated by Fritsch and Hitzig in Germany and by a band of eager spirits in England, which included Jackson, Ferrier and Horsley, to mention only a few. Their studies provided that minimum of information necessary to the beginning of the surgical treatment of those intracranial lesions not visible externally; to permit of the localization of such lesions by deductive reasoning. This beginning was made by Alexander Hughes Bennett, who first so localized an intracranial tumor and persuaded Godlee to operate on it. Sir Victor Horsley, who himself had no small part in the actual experiments which made this development possible, was, however, the first to establish intracranial surgery on a firm basis. Unfortunately, although Horsley's main interest was concerned with the nervous system rather than with surgery, his successors, imitators and pupils were, in the main, general surgeons with little or no interest in the nervous system. They were thus neither interested nor capable of advancing this field of medicine. It is not surprising that at the hands of this disinterested group little or no progress was made in either neurology or neurosurgery. And, as was to be expected, the results of their neurosurgical endeavors were most discouraging. And by the turn of the century the flame of enthusiasm for neurosurgery lit by Horsley in the 1880s was burning very low indeed. At that moment

another dynamic figure, fired by the neurologic experiments that he had performed in Kronecker's laboratory and by the ones he had seen in Sherrington's laboratory at Liverpool, appeared in the *New World*. Harvey Cushing, like Horsley, was not content to deal with the puzzling problems of neurology merely on the basis of existing knowledge. He insisted on personally being in the front line of the attack on neurologic ignorance while at the same time he extended the teachings of Halsted to the field of neurosurgery, masterfully improving its technic as he went. In this same period Charles A. Elsberg in New York and the team of Spiller and Frazier in Philadelphia contributed greatly to the body of knowledge, both technical and diagnostic, in this field. During the six years from the transfer of Cushing from Johns Hopkins to Harvard in 1912 to the close of the war in 1918, intracranial surgery was finally placed on its feet in this country, even though admittedly it toddled rather than walked.

In the ensuing twenty years the members of this branch of the profession have been largely concerned with propagating their kind, with perfecting the technics Cushing gave them and with educating the profession and the public as to their accomplishments. That phase of activity is now largely completed and we seem on the verge of another advance. It is questionable whether we are prepared to make it. We have been so concerned with teaching the young men in this field to execute with reasonable facility the various surgical technics as we now know them that neurosurgeons have been little concerned with seeing that their protégés have had any contact with the basic sciences of anatomy, physiology and pathology, with experimental methods or even with diagnostic neurology. Unbelievable as it may seem, such deficiencies in training are not accidental but often truly deliberate. It would hardly appear necessary to defend the need for the neurosurgeon to be intimately familiar with the structure and function of the part on which he is operating, with the pathologic nature of the lesion which he is treating or to have the ability to recognize clinically not only conditions amenable to the neurosurgical approach but those conditions from which they must be differentiated as well. Yet the chief of one prominent neurosurgical clinic recently said "Why should they know any neurology? They have air and lipiodol, don't they?"

Admittedly in the larger clinical centers it will often be possible for the neurologist and neurosurgeon to work side by side. Such teams, of which that of William G. Spiller and Charles H. Frazier was undoubtedly the most fruitful, have been productive of brilliant results in the past; they may well continue to be so in the future. But such teamwork can be fully productive only when the individuals collaborate on an equal basis. The day has passed when we can tolerate the practice of the days of the barber surgeons, when the

physician stood by and literally directed the hand of an uneducated, though skilful, technician. Furthermore, there exist many situations in which collaboration between neurologist and neurosurgeon either does not or cannot exist. Even in many of the larger centers the patients of the neurosurgeon are never seen by the neurologist. The diagnosis, the decision as to treatment and the treatment itself all being at the hands of one man, the neurosurgeon. Obviously such a man must be fully trained for his task. But the problem confronting our younger men is often even more difficult, and it is with their training that we are primarily concerned here. They are forced to practice in the smaller cities, often being the only individuals in their community at all familiar with the intricacies of the nervous system. They will have thrust on them an extremely variegated picture of neurologic disease, much of which will not benefit from surgical therapy. If they are to meet their obligations to their patients and their medical colleagues they must be trained in more than the technics of the operating theater.

That he who would attack the various diseases of the nervous system with a knife must be a competent surgeon is obvious and of primary importance. But what does competence imply? Merely facile fingers—a certain technical excellence? Certainly more is required of one in whose hands mankind is forced to trust its brains. A detailed familiarity with anatomy has long been one of the prerequisites for the general surgeon. Yet a study of the structure of the nervous system is all too frequently neglected in training the young neurosurgeon. Surely this defect is one which must be a serious handicap to any surgeon so inadequately trained. But a mere familiarity with the structures and how to cut them is not enough. He must know of their functions. As Harvey Cushing said over a quarter of a century ago, "To successfully cope with the many operative problems offered by the various disorders of the nervous system, a man, after a thorough training in pathology and medicine must study, not only in the neurological clinic but also in the laboratory, the pathology of these afflictions in their histological and—what is more important—in their experimental aspects." Such training is essential if he is to diagnose the condition present, to determine its amenability to surgical treatment and to advise the patient and his family as to the possibilities of the future with any accuracy. Surely no less is to be expected of any man who proposes to pose as a specialist within a limited field.

Although such training and knowledge are obviously of the greatest importance to the neurosurgeon's activities as a practicing physician, I am also concerned in this discussion with the relationship of the neurosurgeon and his training to the advancement of neurologic knowledge. In spite of its vast opportunities to study the structure, function and pathology of the human nervous system, which are also new opportunities so far as biology is concerned, neurosurgery has in the past twenty years contributed much less than it might have. True, neurosurgeons have contributed to our knowledge of the cerebrospinal fluid. They have added much to our knowledge of the nature of cerebral neoplasms, although we still have far to go before we shall have reaped the full benefit from such knowledge. They have extended our understanding of the function of the sympathetic nervous system, although this particular line of progress has been marked by numerous errors and retreats which could have been avoided by fuller ana-

tomic and physiologic information and by thoroughgoing experimental exploration. At the present time it is no exaggeration to state that, with the exception of our very limited knowledge of the visual cortex and the precentral motor fields, neurology and neurosurgery are operating largely on a decorticate or even decerebrate level, so far as knowledge of the nervous system is concerned.

Through the years of inspired experimentation by Sir Charles Sherrington and his pupils we have learned much of the functions of the isolated spinal cord and bulb. Recently Larsell, Dow and their associates have organized our knowledge of the structure and function of the cerebellum to a point where for the first time observations regarding this structure made in the laboratory and in the clinic can be reasonably coordinated and understood. Cannon, Bard, Ranson, Beattie and others have done much to bring order out of chaos in our understanding of the hypothalamus, though much remains there to be done. LeGros Clark and Walker have clearly told us the story of the thalamus and pointed the way toward profitable studies of sensation and the afferent innervation of the cerebral cortex. The structure and function of the primate basal ganglions and cerebral cortex, however, are still represented by a great void in our knowledge, and it is here that the neurosurgeon is presented with his great opportunity; but he must be properly trained and intellectually curious if he is to take advantage of it.

In the elucidation of the structure and function of the human cerebral cortex, animal experimentation in a large measure deserts us. The cerebral cortex of no animal is comparable to that of man. If progress toward solution of its mysteries is not to be longer delayed, the neurosurgeon must be equipped to collaborate in its investigation. The cerebral cortex of the dog or cat is vastly different from that of man and, by comparison, relatively unimportant. Except for a severe impairment of vision, its removal is attended with relatively slight change in such an animal. He still walks and runs, he still eats, he may even propagate his kind. The sub-human primates are of considerably more experimental value, but even here great care must be exercised. The monkey, which is the most widely used, is not man in miniature—and observations made on the monkey, from which one precentral region or even one entire cerebral hemisphere can be removed with little more than a fleeting disturbance in the innervation of the skeletal musculature and general behavior, cannot be transferred uncritically to man. Such observations can serve as little more than guideposts in our study of human cerebral physiology. Only the apes, particularly the chimpanzee, approach anywhere near to man in regard to cerebral structure and function. These animals have but rarely been used for the experimental investigation of cerebral physiology except by such investigators as Horsley, Sherrington and more recently in this country by our vice chairman, Prof. John F. Fulton of Yale University. His far reaching observations have taught and are continuing to teach us much of the structure and function of the cerebral cortex. They are pointing the way to the neurosurgeon who must extend and confirm his observations on man. This is the very real responsibility of the neurosurgeon to biology and to mankind. If he is to meet it he must have an understanding of the fundamentals of neurology. Each neurosurgeon will, of course, have his own inclinations and develop them;

and if he does the field of neurology will be notably enriched. He must have a familiarity with scientific experimental methods. He must appreciate the necessity of multiple observations, the necessity for controls and for thoroughgoing and painstaking investigation and observation. If he has these virtues he will not fall victim to superficial observation, as typified by the now notorious conclusion once drawn by a neurosurgeon that "no appreciable mental effects follow the extirpation of both frontal lobes," a conclusion since refuted by a study which required a 350 page monograph to detail all the manifestations produced by such an amputation.

Fortunately it is not necessary to start "at scratch" with such a study. Foerster and his pupil Penfield have made a solid beginning in studying the effects of electrical cortical stimulation on the human brain. Also animal experimentation has taught us much of the structure and function of the precentral region but by no means all. And, furthermore, many of those facts are yet to be confirmed in man. Animal experimentation has also revealed much as to the visual cortex, and the intensive study by Holmes and others of the patients injured during the World War was similarly if less completely illuminating for man. But there we stop. What is known of the frontal lobes and their function? A beginning has been made but only that. We are still talking in the most general terms. Of fundamental mechanisms we are almost wholly ignorant. The parietal lobe is almost in the same state—our knowledge of the mechanism of sensation is distinctly limited to subcortical levels. And the functions of the human parietal lobe, in the main, have yet to be elucidated. Certainly Fulton and his co-workers have shown its relative unimportance in the sensory field in the subhuman primates. The temporal lobe still remains the complete enigma. Klüver and I have made only a beginning which indicates that it is of the greatest importance to the animal's mental and emotional economy. However, these preliminary experiments on the monkey must be correlated with observations on man himself before their full significance can be appreciated.

It should not be concluded that our ignorance regarding the cerebral cortex is confined to function. Far from it. Our knowledge of the afferent and efferent connections of these areas is also inadequate and often erroneous as well.

Is it to be supposed that the neurosurgeon is to turn anatomist, physiologist and psychologist all at once in order that he may solve these problems? Certainly not. But the patients are often his. The opportunities frequently confront him first; often they are of his own making. He must be sufficiently familiar with the entire field of neurology to recognize the opportunity when it appears, to direct it to the best advantage and to collaborate with his colleagues in its fullest utilization. When such collaboration is attained, progress will be made.

Those surgeons who have spent their lives in developing the technique of neurosurgery to its present high level cannot be reproached for their failure to solve these problems. But they must see to it that their successors are so trained that they will be competent to do so. And the remainder of the medical profession, be they administrators of medical organizations and institutions or clinical colleagues in related fields, must place no handicaps in their way to prevent their doing so. It is hoped that they will lend positive aid toward the realization of the ideals herein proposed.

University of Chicago Clinics.

POSTARSPHENAMINE JAUNDICE

APPARENTLY DUE TO OBSTRUCTION OF INTRA-
HEPATIC BILIARY TRACT

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AND

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NEW YORK

Jaundice following administration of arsphenamine ("arsphenamine hepatitis") is usually ascribed to injury of the liver parenchyma. It has been possible in cases terminating fatally to confirm the hepatogenous character of the jaundice by histologic studies, which show marked degenerative changes in the hepatic lobule.¹ In patients with nonfatal jaundice similar though less advanced parenchymal damage is generally assumed to be present and has been demonstrated in a few instances.²

In the course of recent studies employing the serum phosphatase determination and the cephalin flocculation test to differentiate obstructive from hepatogenous jaundice,³ we investigated patients with postarsphenamine jaundice and found as anticipated that the icterus in most instances was of the hepatogenous type. However, results indicative of obstructive jaundice were obtained in some patients, suggesting that icterus following administration of arsphenamine is not always due to liver parenchymal injury but in certain instances is due to obstructive processes within the biliary tract (Hanger³). This distinction in physiologic mechanisms has practical implications bearing directly on the question of the proper approach to treatment.

We have summarized in table 1 twelve cases of postarsphenamine jaundice in which evidence of an obstructive reaction to arsenicals was obtained. The clinical picture so strongly suggested occlusion of the common bile duct that four patients were subjected to exploratory operations. In each instance the extrahepatic biliary tract proved to be patent, but biopsy specimens of the liver revealed marked bile stasis in the finer biliary radicles.

The clinical, chemical and pathologic features of the cases in which intrahepatic obstruction developed are so distinctive that they seem to constitute a discrete disease pattern. The characteristics of this syndrome are illustrated by the three case histories which follow:

REPORT OF CASES

CASE 1.—A white woman aged 51 was treated at the Vanderbilt Clinic for syphilis disclosed by a routine blood Wassermann test. It was stated that no primary or secondary lesions existed; symptoms of tertiary syphilis or neurosyphilis were absent although the spinal fluid gave a positive Wassermann reaction. She received a total of 3.5 Gm. of bismuth subsalicylate from April 17 to May 8, 1939, with no reaction.

From the Department of Medicine, Columbia University College of Physicians and Surgeons and the Presbyterian Hospital.

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TABLE 1.—Summary of Data in Twelve Cases of Postarsphenamine Jaundice Apparently Due to Obstruction of the Intrahepatic Biliary Tract

No. Sex Age Race	State of Syphilis	Therapy and Reactions	Date	Serum				Cephalin Floccula- tion	Bile in Stools	Bile in Urine	Total Duration of Jaundice in Months	Course in Hospital
				Bili- rubin Mg./ 100 Cc.	Phos- phatase, Bodan- sky Units/ 100 Cc.	Choles- terol, Mg./ 100 Cc.						
1 ♀ 51 White	Neuro- syphilis (asymptomatic)	Jaundice developed after third injection of arsphenamine (details in text)	5/31/39 6/12/39 6/16/39 6/22/39 6/26/39 6/29/39	5.3 13.6 16.6 15.6 13.7 12.0	19.5 42.7 41.6 33.9 25.1 25.0	204 ... 642 1,120 1,100 1,310	± 0 0 0 0 0		Clay colored for weeks	++	3½	Details in text
2 ♂ 43 White	Latent	Jaundice developed after second injection of neoarsphenamine (details in text)	7/29/39 8/ 7/39 8/15/39 8/22/39 8/31/39	16.0 16.5 13.0 6.6 3.6	10.0 9.0 10.0 9.3 8.4	165 203 219	0 0 0 0 0	Gray or light brown	++++		6	Details in text
3 ♂ 29 White	Neuro- syphilis (asymptomatic)	Jaundice developed after second injection of neoarsphenamine (details in text)	5/20/38 6/ 1/38 6/14/38 6/21/38 7/ 6/38	17.0 15.0 12.5 9.4 2.0	17.6 13.8 11.6 11.8 ...	580 487 488	0 0 0 0 0	Tan	+++		2½	Details in text
4 ♀ 36 Negro	Latent	Bismuth weekly June '37-April '38, no reaction; 4/22/38, bismuth and first neoarsphenamine (0.6 Gm.), no reaction; within 8 hours after second neoarsphenamine (0.6 Gm.), 4/29/38, chills and vomiting, then malaise, weakness; one week later jaundice, itching, light stools, loss of weight	7/26/38 8/ 4/38 9/ 1/38 9/13/38 9/27/38 10/19/38 12/ 9/38	10.4 8.3 15.0 11.7 9.4 5.9 2.0	12.7 ... 18.5 20.1 13.9	254 235	0 0 0 0 0 0 0	Intermittently tan and clay colored for months	++		7	Intractable itching persisted and was the presenting symptom; fever 99-100 F. for 6 weeks, no gastrointestinal symptoms except anorexia; complete recovery
5 ♀ 22 White	Secondary (rash)	Bismuth May 2, 7, 15, 1935, no reaction; first neoarsphenamine (0.3 Gm.) 5/10/35, no reaction; second arsphenamine (0.3 Gm.) 5/18/35; several hours later, chills, fever, malaise; three days later dermatitis, fever, vomiting; then facial edema, jaundice, itching, light stools; third neoarsphenamine 6/1/35; that night, acute exacerbation	6/ 2/35 6/10/35 6/18/35	11.0 7.5 4.8	... 43.0 43.7	... 476 472	..	Tan	+		1	Rapid subsidence of all symptoms but jaundice; complete recovery
6 ♀ 33 Negro	Tertiary (syphilitic)	Bismuth weekly two months, no reaction; first arsphenamine (0.1 Gm.) 3/24/36, questionable reaction; second arsphenamine (0.15 Gm.) 4/1/36; that night chill, fever, vomiting, malaise; next day rash, conjunctivitis, facial edema; then joint pains, diarrhea; after four days jaundice	5/10/36 5/18/36 6/ 4/36 6/28/36	6.0 11.0 6.8 2.0	... 15.8	Tan	+		2¾	Rapid subsidence of symptoms except cutaneous lesions, which cleared after 2 weeks, and jaundice, which persisted; complete recovery
7 ♂ 35 Chinese	Syphilitic?	First neoarsphenamine (0.3 Gm.) 3/9/39, no reaction; first bismuth (0.1 Gm.) 3/14/39, no reaction; second neoarsphenamine (0.4 Gm.) 3/18/39, no immediate reaction; that night chills, headache, malaise; neoarsphenamine and bismuth discontinued, then bismuth given twice weekly; jaundice noted in about two weeks after second neoarsphenamine	7/24/39 7/28/39 8/18/39 9/ 6/39 10/ 4/39 10/25/39 11/ 7/39 11/14/39 11/25/39 12/11/39 12/26/39 1/ 9/40 1/22/40	6.5 6.5 4.7 4.0 10.7 5.0 15.0 7.5 6.1 4.0 5.0 8.3 19.0	16.7 14.9 24.7 18.1 25.3 32.5 34.8 35.4 33.7 35.2 26.6 50.2 38.4	159 ... 253 313 337 755 1,250 1,400 1,650 2,400 2,800 3,100 3,050	0 0 0 0 0 0 0 0 0 0 0 0 0	Intermittently tan and clay colored for months	++++	>7	Jaundice, itching, weight loss the presenting symptoms for months; exploratory operation 8/2/39, no obstruction of common duct found (details in text); transient improvement postoperatively; then recurrence of painless afebrile jaundice due to post-operative adhesions; (exploratory operation 2/6/40)	
8 ♂ 36 White	Latent	Bismuth weekly 3 months, no reaction; first arsphenamine (0.1 Gm.) 4/1/36, no reaction; second arsphenamine 4/8/36 (0.2 Gm.), four hours later conjunctivitis; third arsphenamine (0.3 Gm.) 4/15/36, several hours later itching rash on hands; next day nausea, vomiting, jaundice	4/18/36 4/22/36 4/27/36 5/ 8/36 5/15/36	5.6 8.3 8.3 4.3 3.0	... 24.6 17.1 ... 10.4	Acholic two weeks then tan	++		1½	Rapid subsidence of symptoms except jaundice; complete recovery
9 ♂ 19 Negro	Latent	One preliminary bismuth injection, no reaction; first arsphenamine 2/14/38, local reaction only; second arsphenamine 2/21/38, after 2 hours malaise, fever, itching; third arsphenamine 3/2/38, after 1 hour vomiting, then fever, conjunctivitis, arthralgia, weakness; then jaundice	3/ 9/38 3/16/38 3/22/38	7.0 8.2 2.2	12.2 ... 14.3	213 325 ...	±	Brown	+++		¾	Rapid subsidence of symptoms except jaundice and persistent temperature of 100 F.; complete recovery

TABLE 1.—Summary of Data in Twelve Cases of Postarsphenamine Jaundice Apparently Due to Obstruction of the Intrahepatic Biliary Tract—Continued

No. Sex Age Race	State of Syphilis	Therapy and Reactions	Date	Serum				Bile in Stools	Bile in Urine	Total Dura- tion of Jaundice in Months	Course in Hospital
				Bili- rubin Mg./ 100 Cc.	Phos- phatase, Bodan- sky Units/ 100 Cc.	Choles- terol, Mg./ 100 Cc.	Cephalin Floccula- tion				
10 ♀ 24 Negro	Latent	Therapy started 3/7/39, bismuth and 0.15 Gm. arsphenamine; anorexia 2 days, sensitive gums; 3/13/39, bismuth and second arsphenamine (0.15 Gm.), later vomiting and questionable jaundice; 3/20/39, bismuth and third arsphenamine (0.2 Gm.), that night chills, fever, vomiting; then diarrhea, abdominal pain, light stools, arthralgia; after 3 days, jaundice, itch	3/27/39 4/ 3/39	7.9 11.5	10.8 20.4	177 347	++++ ++	Gray one week	++	>1½	Gradual subsidence of acute symptoms, persistent jaundice and intractable itching presenting complaints; last seen May 1939, still icteric
11 ♂ 24 Negro	Latent	Received 5 weekly bismuth injections beginning 8/11/33, no reaction; also arsphenamine 0.15 Gm. 8/12/33, 0.25 Gm. 8/17/33, 0.25 Gm. 8/24/33 and 0.2 Gm. 9/5/33; several hours after second arsphenamine, weakness, vomiting, dizziness, feverish; exacerbation of these symptoms with rash on shoulders, itching several hours after third injection; after fourth injection, same plus marked jaundice, diarrhea, clay-colored stools, crampy abdominal pains	9/27/33 10/14/33 11/ 2/33 11/14/33 11/27/33	21.4 16.2 17.9 8.3 9.1 250	Clay colored one month	++++	>2½	All acute symptoms soon subsided, jaundice and intractable pruritus persisting; explored 11/3/33, no obstruction of common duct found (details in text); complete recovery
12 ♂ 23 Puerto Rican	Primary	Received 0.2 Gm. arsphenamine and bismuth 1/2/40; slight reaction; 1/4/40, 0.2 Gm. arsphenamine; 1/12/40, 0.3 Gm. arsphenamine and bismuth; 1/16/40, 0.4 Gm. arsphenamine and bismuth; several hours after second and third injections chill, fever, malaise, nausea; after fourth injection, same with vomiting, abdominal pain, then jaundice with dark urine, light stools, slight itching	1/26/40 1/31/40 2/ 5/40 1/13/40	7.5 15.0 10.5 7.5	26.9 41.9 30.0 22.6	263 411 390 450	0 0 0 0	Tan two weeks then brown	+++	>1	Acute symptoms soon subsided, jaundice and itching persisted; still under observation

May 15 she was given 0.1 Gm. of arsphenamine intravenously, with no reaction. May 22 she received a second injection of 0.15 Gm. of arsphenamine, with no immediate reaction. Six hours later, however, she had a shaking chill and throughout that night she suffered alternate chills and fever, without nausea or vomiting. The next morning she complained of anorexia, drowsiness and weakness but could resume her work as laundress. Several days later she noted transient dark urine and itching of the skin but was not aware of icterus or of acholic stools. She said nothing of these symptoms on returning to the clinic May 29 and received a third injection of 0.2 Gm. of arsphenamine. There was no immediate reaction but a half hour later she had a shaking chill, became nauseated, dizzy and weak and complained of generalized muscle aches. Icteric scleras were noted. There was no abdominal pain at the onset or throughout the course of her illness. She gave no history of gallbladder disease or antecedent jaundice; there was no preceding infection of the upper respiratory tract or dietary indiscretion. There was no history of allergy.

The patient was admitted at once to the Presbyterian Hospital acutely ill and mentally confused, with a temperature of 104 F., pulse rate of 100 and normal blood pressure. Jaundice was marked. An erythematous rash was present on the forearms. The only syphilitic stigmas found were typical Argyll Robertson pupils. The liver and spleen were not enlarged or tender. The hemoglobin and red cell count were normal; the white cell count was 16,600 with 93 per cent polymorphonuclear cells. The sedimentation rate was 45 mm. in one hour. The urine contained bile and albumin (2 plus). The stools were clay colored.

The patient was placed on a high carbohydrate, low fat diet. The fever subsided in four days as did the other symptoms except pruritus, which was the most distressing complaint. The

stools remained clay colored for weeks, intermittently showing occult blood. Chemical examination of the blood (table 1) revealed increasing serum bilirubin levels for three weeks (reaching 16.6 mg. per hundred cubic centimeters), associated with serum phosphatase values as high as 42.7 Bodansky units per hundred cubic centimeters, and consistently negative results with the cephalin flocculation test. The serum cholesterol level, which was normal at the outset, rose to over 1,000 mg. per hundred cubic centimeters one month after the onset of jaundice. The hippuric acid test yielded a value of 2.3 Gm. (slightly below the normal minimum value) after three weeks of intense jaundice. Duodenal drainage on several occasions failed to show bile. Roentgenograms of the gallbladder were equivocal as regards the presence of radiopaque stones.

Despite the close correlation with arsenical administration, the clinical and chemical picture was so typical of obstructive jaundice that surgical intervention was contemplated. However, the serum bilirubin and phosphatase levels began to fall about one month after the onset of jaundice, so that conservative management was continued. Slow improvement was noted until the jaundice finally cleared after three and one-half months.

CASE 2.—A previously healthy white man aged 43 consulted his family physician in March 1939 for difficulty in vision. A positive Wassermann reaction was discovered; it was stated that primary and secondary lesions were absent. His physician gave an intravenous injection (probably neoarsphenamine, dosage not known), without untoward reaction. One week later a second intravenous injection was given, with no immediate reaction. But some ten hours later he had a shaking chill lasting about two hours. There was no feverishness and no gastrointestinal or cutaneous reaction. Jaundice appeared on the second day and rapidly became more intense. This was associated with distressing itching and with some

anorexia but no other complaints. About this time the urine became dark and the stools gray. After four weeks there was some darkening in the color of the stools, associated with transient lessening in the intensity of jaundice. He lost 30 pounds (14 Kg.) in the nine week period prior to hospitalization. During this time he was on a high carbohydrate, low fat diet. On admission to the Presbyterian Hospital July 28 the presenting symptoms were intense jaundice and obvious weight loss; the chief complaint was intractable pruritus. The temperature, pulse and blood pressure were normal. The liver edge was palpable 6 cm. below the costal margin and was very firm but not tender. The spleen could not be felt. There was no evidence of cardiovascular syphilis or neurosyphilis. The erythrocyte, hemoglobin and leukocyte content of the blood were all within normal limits. The urine contained bile, a trace of albumin and a few granular casts. The stools were greenish gray but gave a positive reaction to a Schmidt test for bile pigment. Roentgenograms of the gallbladder were negative for radiopaque stones.

The patient was maintained on a high carbohydrate, low fat regimen, also receiving 15 per cent dextrose solution intravenously at frequent intervals. His condition remained unchanged: afebrile, with painless jaundice of undiminished intensity and intractable pruritus. The serum bilirubin continued at a level of about 16 mg. per hundred cubic centimeters, the serum phosphatase fluctuated around 10 Bodansky units per hundred cubic centimeters, and the cephalin flocculation test gave consistently negative results (table 1). August 7, after almost five months of jaundice, an exploratory operation for obstruction of the common bile duct was performed. The common duct was patent and not dilated. A punch biopsy specimen of the liver was obtained (data will be given later). The pathologic diagnosis was chronic cholecystitis, chronic cystic lymphadenitis and cholangitis.

About a week after operation, the jaundice and itching began to diminish and thereafter convalescence was rapid. The stools began to show more bile pigment two weeks after operation and continued to be brown. He was discharged August 31, still slightly icteric, the total duration of jaundice in this instance being about six months.

CASE 3.—A Syrian aged 29 consulted his family physician in March 1938 for care of acute tonsillitis, also requesting a blood Wassermann test, which was positive. It was stated that primary and secondary lesions were absent. April 12, having recovered from his sore throat, he was given 0.45 Gm. of neoarsphenamine. There was no immediate reaction, but several hours later transient weakness and profuse perspiration developed. April 19 the patient received a second intravenous injection of 0.45 Gm. of neoarsphenamine, with no immediate reaction. Four hours later he had a weak spell with a shaking chill, vomited and went to bed (where he remained until hospitalized). The next day fever, nausea and vomiting developed, and jaundice was noted by his physician. The eyes became puffy and red, his "whole body was swollen," and there was moderate diffuse discomfort in the lower part of the abdomen. These symptoms soon subsided, but anorexia persisted and the jaundice deepened. The urine was very dark and the stools light colored; itching appeared and grew steadily worse. Vague muscle pains were noted, particularly marked in the legs. There was no diarrhea at any time. He gave no history of previous antisyphilitic therapy; there was no antecedent jaundice or dietary indiscretion and nothing to suggest gallbladder disease; no history of allergy was given.

When admitted to the Presbyterian Hospital May 19, one month after onset, he was deeply jaundiced and complained chiefly of itching. The temperature was 100 F.; the pulse, respirations and blood pressure were normal. The left pupil was irregular and reacted sluggishly to light and in accommodation (subsequent lumbar puncture showed neurosyphilis); the reflexes were intact. There was no clinical evidence of cardiovascular syphilis. The liver edge was palpable two fingerbreadths below the costal margin but not tender; the spleen was just palpable. The hemoglobin level was 13 Gm. per hundred cubic centimeters; erythrocytes numbered 3,700,000 and leukocytes 7,700, of which 68 per cent were neutrophils, 19 per cent lymphocytes, 4 per cent monocytes, 1 per cent basophils, 3 per cent myelocytes and 5 per cent eosinophils. The

platelets numbered 357,000. Reticulocytosis with the count varying from 6 to 18 per cent was noted during the first two weeks. The red cell fragility in saline solution was normal. The erythrocyte sedimentation rate was 113 mm. in one hour. The urine contained bile but no albumin. The stools were light tan and gave negative mercuric chloride reactions for bile. X-ray examinations showed no radiopaque stones in the gallbladder. Duodenal drainage yielded no B bile and no cholesterol or calcium bilirubinate crystals.

The patient was placed on a high carbohydrate, low fat regimen, with forced fluids, vitamin B₁ given intravenously and liver extract intramuscularly. He continued to have a temperature of 100 F., at first consistently then intermittently, throughout his eight week stay in the hospital. During this period, itching remained the presenting complaint, gastrointestinal symptoms being minimal. The stools remained light in color and gave negative results in mercuric chloride tests for bile for the first six weeks. The erythrocyte sedimentation rate remained elevated up to the time of discharge, when it was 53 mm. in one hour. The eosinophilia persisted, but the reticulocytes and myelocytes disappeared after one month. Chemical studies of the blood (table 1) showed serum bilirubin values as high as 17 mg. per hundred cubic centimeters on admission, with a very gradual decline to the slight elevation present at discharge. The serum phosphatase was definitely increased; repeated cephalin flocculation tests gave negative results. The serum cholesterol values were elevated. A moderate and persistent increase in serum globulin (3.1 per cent) was noted. A hippuric acid test May 24, after more than a month of jaundice and at a time when bilirubinemia was very marked, yielded 2.2 Gm., expressed as benzoic acid.

The patient was discharged July 12, free of symptoms, after some two and one-half months of jaundice. His subsequent course has been uneventful.

CLINICAL CHARACTERISTICS OF POSTARSPHENAMINE JAUNDICE APPARENTLY DUE TO OBSTRUCTION OF THE INTRAHEPATIC BILIARY TRACT

In every case included in table 1 jaundice developed during the first course of treatment with intravenous arsenicals, irrespective of whether or not this was preceded or accompanied by bismuth therapy. With few equivocal exceptions, the first intravenous injection was without incident, but reactions of the type under consideration invariably occurred after the second or third intravenous injection of either arsphenamine or neoarsphenamine, in moderate or small dosage. There was nothing else of etiologic significance in the antecedents of most patients: none had been jaundiced before or had had definite symptoms of cholecystitis or cholelithiasis, none admitted dietary indiscretion preceding the onset of jaundice, and none had previously received arsenicals. Patients 3, 8 and 11 had mild infections of the upper respiratory tract shortly before or during their course of treatment. In only one instance (case 9) was there any swelling at the site of injection, and in none was there any immediate, "nitritoid" reaction to suggest errors in the technic of administration or in the substance administered. Patient 11 gave a definite history of allergy; patient 8 gave an equivocal allergic history. In case 7 cholecystectomy two months prior to the appearance of jaundice suggested stricture of the common bile duct as the cause of icterus, but this possibility was excluded by exploration. No correlation with age, sex, race or stage of syphilis could be made out; in at least one instance (case 7) the diagnosis of syphilis was open to doubt because of repeatedly negative Wassermann tests after little treatment.

The reaction in this group of patients was of the delayed type, the usual interval between injection and the appearance of symptoms being from two to ten hours. In those subjects who had symptoms after the second injection but received further treatment never-

theless, the reaction came on more rapidly (within an hour in cases 1 and 9) and more violently. The onset of symptoms in most patients was acute, characteristically initiated by shaking chills and fever with malaise, headache and vertigo and followed after a variable period by anorexia, nausea and vomiting. Some patients did not have chills, the reaction beginning with a gastro-

Choluria, acholic or hypocholic stools and itching were observed generally at about the time icterus appeared. With the persistence of jaundice and gastrointestinal symptoms (notably anorexia), marked asthenia and considerable weight loss developed as in cases 2 and 4, in which over 30 pounds was lost in the first two months of illness. Marked dehydration in cases 5 and 6 resulted

TABLE 2.—Summary of Data in Eight Cases of Postarsphenamine Jaundice; Typical of the Usual Picture (Consistent with Hepatitis)

No. Sex Age Race	State of Syphilis	Therapy and Reactions	Date	Serum				Bile in Stools	Bile in Urine	Total Duration of Jaundice in Months	Course in Hospital
				Bili- rubin Mg./ 100 Cc.	Phos- phatase Bodan- sky Units/ 100 Cc.	Choles- terol, Mg./ 100 Cc.	Cephalin Floccula- tion				
13 ♀ 35 Negro	Latent (syphili- tic?)	Six weekly intravenous injections (probably neoarsphenamine) Feb.-March 1938, no reactions; in May 1938, two months after last injection, noted painless jaundice, anorexia, light stools, then diarrhea; no preceding cold, etc.	6/ 3/38 6/13/38 6/27/38 7/ 5/38	13.0 9.4 5.0 4.3	6.9 8.7 8.9 8.6	150 94 69 74 +++	Brown	+	2	Fever (to 100 F.) for 3 weeks, mild gastrointestinal symptoms; little itching; hippuric acid test, 0.53 Gm. excreted; complete recovery
14 ♀ 43 White	Lateot (syphili- tic?)	Intravenous specific therapy 10 years before (1927); no symptoms referable to syphilis, negative Wassermann in 1937 but given silver arsphenamine (total 2.1 Gm.) May-July 1937, no reactions; 11/24/37, 4½ months after last injection, jaundice, aches, anorexia; no preceding cold, etc.	12/ 3/37 12/15/37 12/21/37	11.7 10.1 9.4	7.3 5.4 ...	250 ++++	Clay colored or tan first weeks	+	1½	Afebrile, no marked gastrointestinal symptoms, no pain or itching; complete recovery
15 ♂ 46 White	Latent	Specific treatment 4 years (6 courses arsphenamine, 9 courses bismuth compound) beginning 1935; while under treatment June 1939, jaundice, nausea, asthenia; recovery but recurrence of jaundice after 1 arsphenamine injection Dec. 1939	12/ 8/39 12/22/39	7.0 2.0	7.4 6.4	... 188	+++	Brown	++	½	Malaise, no itching; complete recovery
16 ♂ 42 Negro	Tertiary (cardio- vascular)	Twelve bismuth injections, then started arsphenamine June 1937; discontinued after 4 intravenous injections because of abdominal distention, vomiting, diarrhea; several weeks after last injection, jaundice, asthenia, light stools; no preceding cold, etc.	7/24/37 7/27/37 7/29/37 8/ 2/37	15.1 7.5 4.8 2.9 4.1 ++++	Light brown	++	1½	Afebrile; gastrointestinal symptoms 3 weeks, rapid decrease in jaundice, no itching; complete recovery
17 ♀ 25 Negro	Latent	Beginning March 1939, 3 bismuth then 9 arsphenamine injections, no reactions; after tenth injection, vomiting, weakness, three days after eleventh injection (6/2/39), jaundice, vomiting; no preceding cold; (pregnant, 4th month, March)	6/ 8/39	17.0	14.5	183	+++	Brown	++	1½	Pregnancy, 7th month premature labor; jaundice asymptomatic, no fever; complete recovery
18 ♂ 46 White	Tertiary (cardio- vascular)	Intermittent intravenous specific therapy 1920-1937, no reactions; caught cold while receiving silver arsphenamine June 1937, jaundice, vomiting promptly developed	6/14/37 6/21/37	4.2 3.0	8.2 6.2	144 +	Brown	0	1	Afebrile, few symptoms; suspected Laennec cirrhosis; complete recovery
10 ♀ 23 Negro	Secondary	June 1935, 3 weekly intravenous injections probably neoarsphenamine, 1 bismuth; no reactions; Sept. 1935, painless jaundice, light stools, itching, asthenia; no preceding cold	9/22/35 10/ 4/35 10/14/35	15.3 12.2 5.2	4.9 4.2	Light brown	++++	2	Afebrile, slight anorexia; galactose test, 7 Gm. excreted; complete recovery
20 ♂ 37 Negro	Latent	Weekly intramuscular and intravenous therapy for one year beginning Oct. 1935; in Dec. 1936, 2 months after last injection, caught cold; abdominal distention, jaundice, light stools noted shortly thereafter	1/14/37 1/20/37 1/29/37	15.0 14.2 5.6	7.5 4.9 4.1	Brown	++	1	Fever of 99 F., otherwise asymptomatic jaundice; complete recovery

intestinal upset, or as "conjunctivitis" with chemosis, or as dermatitis. A transitory morbilliform or scarlatiniform eruption appeared early on the upper extremities and trunk in six cases, subsequently becoming more extensive in several instances. Diffuse muscle pains and fleeting arthralgias were severe enough in four cases to constitute a major early complaint. Diarrhea, crampy abdominal pains and edema of the face or extremities developed in the first days of illness in several instances.

Jaundice did not appear until one or more days after the onset of symptoms, some patients (particularly Negroes) failing to note it for periods exceeding a week.

from fluid loss through vomiting, diarrhea and diaphoresis. Enlargement of the liver with extension from 3 to 6 cm. below the costal margin was noted in four patients, associated with slight splenic enlargement in patients 3 and 5. A moderate hypochromic anemia was present in cases 3 and 5. Initial leukocyte counts ranging from 19,000 to 12,500 with 93 per cent neutrophils were observed in acutely ill, febrile patients (patients 1, 5, 6). In cases 3, 10 and 11 there was eosinophilia with a level of 5 to 12 per cent; in case 9 the eosinophilia reached a level of 21 per cent and, in case 12, 50 per cent. The blood in case 3 showed myelocytes ranging

to 6 per cent and reticulocytosis with values from 6 to 18 per cent during the first two weeks of hospitalization; reticulocyte counts to 4 per cent were also observed in case 5. Moderate to very marked increases in the erythrocyte sedimentation rate were noted in every case. Serologic tests for syphilis were positive in all instances except in case 7, although the infection appeared to be latent in many of the cases (table 1). The urine invariably contained bile pigment and in the earlier phases of illness in cases 1, 2, 5, 6 and 10 also contained faint to heavy traces of albumin. As indicated in table 1, the majority of patients showed little or no bile in the stools. Occult blood appeared in the stools in cases 1, 7 and 12. Gallbladder roentgenograms and duodenal drainage for evidences of stones uniformly gave negative results.

The acute constitutional and gastrointestinal symptoms initiating the reaction subsided after a few days or weeks, although in some instances low grade fever, anorexia or weakness continued. The later course of the reaction was characterized by painless jaundice of unusual duration (more than six months in cases 2, 4 and 7); and by relative freedom from associated symptoms except for the frequent occurrence of intense pruritus. The diminished bile content of the stools persisted and in many cases (table 1) was of such

intercurrent colds, dietary indiscretions and the like that the chief role of arsphenamine may be to predispose the liver to "catarrhal" jaundice.

CHEMICAL CHARACTERISTICS OF POSTARSPHENAMINE JAUNDICE APPARENTLY DUE TO OBSTRUCTION OF THE INTRAHEPATIC BILIARY TRACT

As already indicated, we have employed the serum phosphatase determination (Flood and others,³ Gutman and others³) and the cephalin flocculation test (Hanger³) to differentiate obstructive from hepatogenous jaundice. According to our experience (table 3), serum phosphatase levels greater than 10 Bodansky units signify that the icterus is probably of the obstructive type whereas values less than 10 Bodansky units point toward hepatitis. Applying this experience to the interpretation of our results in patients with postarsphenamine jaundice, we find that of the eleven cases in table 1 investigated, in ten there were serum phosphatase values greater than 10 Bodansky units per hundred cubic centimeters, i. e. levels consistent with obstructive jaundice. Of twenty-three other cases of postarsphenamine jaundice in which we have serum phosphatase determinations, cases not conforming to the syndrome of table 1, in eighteen serum phosphatase

TABLE 3.—Results of Serum Phosphatase Determination and Cephalin Flocculation Test in Obstruction of the Extrahepatic Biliary Tract, in "Catarrhal" Jaundice and in Postarsphenamine Jaundice

	Serum Phosphatase Activity *			Cephalin Flocculation Test					Negative or ±
	Number of Adult Cases Studied	Number with Values of 10.0 or More	Number with Values Less Than 10	Number of Adult Cases Studied	++++	+++	++	+	
1. Jaundice due to obstruction of the extrahepatic biliary tract (carcinoma head of pancreas, etc.).....	79	72	7	77	0	0	1	6	70
2. "Catarrhal" jaundice (not due to known toxic agents).....	69	7	62	60	37	11	6	2	4
3. Postarsphenamine jaundice (clinical history consistent with obstructive type).....	11	10	1	8	1	0	0	0	7
4. Postarsphenamine jaundice (clinical history consistent with hepatogenous type).....	23	5	18	7	2	3	0	1	1

* Serum phosphatase results expressed in Bodansky units per hundred cubic centimeters.

degree and duration as is rare except in obstructive jaundice. Eventually, the patients included in table 1 made an apparently complete recovery. Patient 10 was lost to follow-up study before the jaundice had disappeared entirely; patients 7 and 12 are still under observation.

By way of contrast with the clinical picture presented by the cases comprising table 1, we have summarized in table 2 the data of eight representative patients with postarsphenamine jaundice due to liver parenchymal degeneration ("hepatitis"). In the latter heterogeneous group of cases, jaundice may develop at any time during or after courses of treatment; there is no consistent relationship between the number of arsenical injections received and the appearance of symptoms. The reaction rarely begins so acutely, with shaking chills and fever. The clinical picture ordinarily is not that of obstructive jaundice, as in the cases in table 1, but is more consistent with hepatitis, often indistinguishable from that of "catarrhal" jaundice. In fact, as many investigators have emphasized,⁴ icterus so frequently develops after

values were less than 10 Bodansky units, i. e. levels consistent with hepatogenous jaundice. The five exceptions include one case in which jaundice was shown at autopsy to be due to carcinoma of the head of the pancreas and not to the arsphenamine received; in another there was a late stage of pregnancy (case 17), and in the remainder there was an underlying Laennec cirrhosis, all factors which independently may cause increased serum phosphatase activity.

The cephalin flocculation test (table 3) has been carried out in seventy-seven cases of obstruction of the extrahepatic biliary tract, in seventy-six with negative or weakly positive reactions. Of sixty patients with "catarrhal" jaundice so tested, fifty-four gave definite flocculation whereas only six gave negative or 1 plus results, the latter chiefly patients first tested while jaundice was subsiding. Applying this experience to the interpretation of our results in postarsphenamine jaundice, we find that of the eight patients in table 1 subjected to this test, seven gave negative results, i. e. no evidence of liver parenchymal damage was obtained. On the other hand, of seven patients with postarsphenamine jaundice who did not fall in the group included in table 1, five gave 3 plus or 4 plus reactions, i. e. results consistent with jaundice of the hepatogenous type. The two exceptions were not tested until late in

4. Herxheimer, Gotthold, and Gerlach, Werner: Ueber Leberatrophie und ihr Verhältnis zu Syphilis und Salvarsan. Beitr. z. path. Anat. u. z. Allg. Path. 68: 93, 1921. Ruge, Heinrich: The Connection between Syphilis, Salvarsan and So-Called Catarrhal Jaundice on the Basis of 2,500 Cases Observed in the German Navy from 1919 to 1929, Urol. & Cutan. Rev. 36: 355 (June) 1932. Wile, U. J., and Sams, W. M.: A Study of Jaundice in Syphilis: Its Relation to Therapy, Am. J. M. Sc. 187: 297 (March) 1934.

the course of their illness when their jaundice was already subsiding and when the test is of little diagnostic value.

As is well known, the total cholesterol content of the blood serum tends to rise in patients with obstructive jaundice whereas normal or low values are observed in

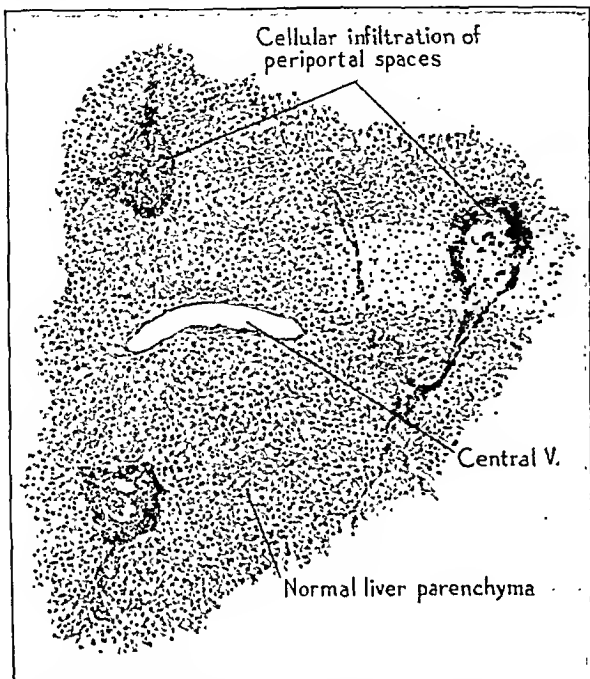


Fig. 1 (case 2).—Drawing of a low power field showing cellular infiltration of three periportal areas and normal liver parenchyma.

patients with jaundice due to hepatitis. Determinations of the total serum cholesterol were made for ten of the patients in table 1, of whom all but one (patient 2) showed levels of 250 mg. per hundred cubic centimeters or over while under observation, and in some instances extraordinarily high values were obtained. For reasons not apparent, the upward trend in serum cholesterol levels usually became more marked in the recovery phase of illness, when the serum bilirubin values began to fall. For patients with postarsphenamine jaundice not of the type included in table 1, normal or low cholesterol values were obtained (table 2), as in "catarrhal" jaundice.

A few "liver function" tests were performed and the results were consistent, on the whole, with the data already recorded. In cases 1, 3 and 12 values were 2.3, 2.2 and 5.3 Gm., respectively, with the hippuric acid test, as compared with 0.83 Gm. in case 13 of table 2.⁵ Case 11 yielded a value of 0.87 Gm. with the galactose excretion test, as compared with 7.0 Gm. in case 19 of table 2. A slight rise in serum globulin to a level of from 3.0 to 3.5 Gm. per hundred cubic centimeters occurred in almost all cases in table 1, particularly in the late stages; this was associated with a moderate fall in serum albumin, so that the total serum protein values remained within normal limits. No significant increase in nonprotein nitrogen of the serum was noted. The arsenic content of the blood (in milligrams per hundred grams of dry blood) was determined in case 1 (trace), case 6 (0.1 mg.), case 10 (0.50 mg.) and case 11 (0.18 mg.), the normal range being from 0.01 to 0.08 mg.

5. Dr. Bruce Hogg furnished these values.

PATHOLOGIC FEATURES IN POSTARSPHENAMINE JAUNDICE APPARENTLY DUE TO OBSTRUCTION OF THE INTRAHEPATIC BILIARY TRACT

In cases 2, 7, 11 and 12 of table 1 operation and liver biopsies were performed. Dr. Alwin M. Pappenheimer and Dr. Virginia Kneeland Frantz gave the histologic descriptions, and Dr. Paul Klemperer reviewed the sections.

CASE 2.—At operation the liver was enlarged, not particularly firm and slightly darker than normal. The common duct was not obstructed or dilated and contained viscid bile. Several enlarged soft cystic lymph glands were seen. The gallbladder walls were somewhat pale and thickened and contained inspissated bile but no stones. Cholecystectomy was done, but subsequent microscopic examination revealed only mild chronic inflammatory changes.

Biopsy of the liver showed fair preservation of architecture. The liver cells appeared normal with vacuolations suggesting glycogen. There was slight but definite increase in fibrous tissue about the central veins and in the portal areas. A few proliferating bile ducts were seen. There was considerable inflammatory infiltration of the portal areas, chiefly lymphocytic with some polymorphonuclears (figs. 1 and 2). Polymorphonuclear cells were found within the walls and around the finer biliary radicles. The most striking feature of the section was the presence of patchy areas in which the bile canaliculi were markedly distended with bile plugs (fig. 3). Many Kupffer cells had taken up bile pigment. The diagnosis was pericholangitis and cholangiolitis.

CASE 7.—At operation Aug. 2, 1939, the liver was considerably enlarged. It seemed firmer than normal and was faintly bile stained, with a finely granular surface. The common duct was patent and of normal caliber. It contained a small amount of normal appearing bile.

Biopsy of the liver showed normal architecture. No necrosis of liver cells was seen. In some areas the liver cells and their nuclei were of larger than average size and stained more

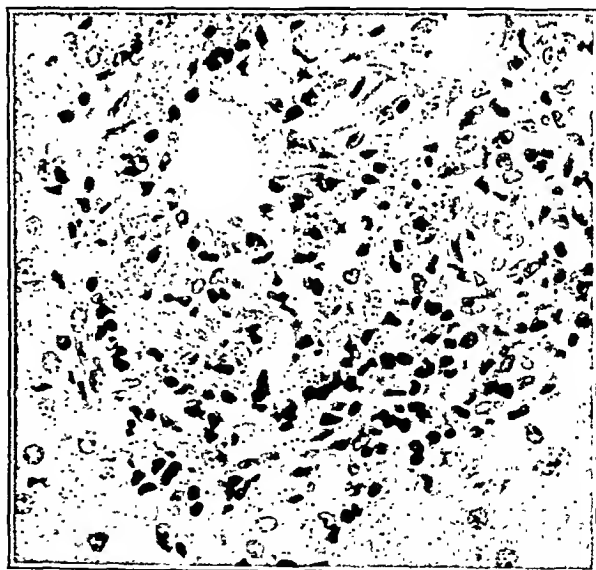


Fig. 2 (case 2).—Section of portal area showing infiltration with mononuclear and polymorphonuclear cells (high power).

intensely with eosin. The portal areas were extensively infiltrated by lymphoid cells and by moderate numbers of polymorphonuclears. There were many polymorphonuclear cells within the walls and around the finer biliary radicles. Peribiliary connective tissue was not increased. There was marked stasis of bile as indicated by many large plugs in the canaliculi (fig. 4). Many of the Kupffer cells were loaded with bile pigment. The diagnosis was pericholangitis and cholangiolitis.

CASE 11.—At operation the liver was slightly enlarged, smooth and dark gray with a fine brownish mottling. The common duct was not obstructed or dilated. A large firm lymph gland was present at the junction of the cystic and common ducts. The gallbladder was adherent to the colon, was not distended and contained no stones.

Biopsy of the liver showed normal architecture. Except for sporadic cells showing homogeneous eosinophilic cytoplasm and nuclear degeneration, the liver cells appeared to be normal. There was no portal fibrosis. Bile plugs were present in many bile capillaries. In the portal areas there were scattered lymphocytes and occasional polymorphonuclears and eosinophils. There was some polymorphonuclear infiltration of the walls of the finer biliary radicles. Large mononuclear cells filled with bile were found near the central veins. The Kupffer cells also contained bile. The diagnosis was pericholangitis and cholangiolitis.

CASE 12.⁶—A specimen of liver for biopsy was obtained by aspiration² three weeks after the onset of jaundice.

The architecture of the liver was normal. There was no necrosis of the liver parenchyma. There was less cellular infiltration of the portal areas than in the preceding cases, but abnormal accumulations of round cells and polymorphonuclears and eosinophils were noted. The most striking feature was dilatation and engorgement of the finer biliary radicles with bile. A few of the liver cells and Kupffer cells contained bile pigment.

The essential features of the liver biopsy sections were (1) absence of significant parenchymal degeneration in intensely jaundiced patients; (2) cholangiolitis and pericholangitis of the nonsuppurative type (no infection of the biliary tree could be demonstrated), and (3) the presence of bile plugs in many of the bile capillaries, suggesting that the finer biliary radicles were the chief site of injury. Inflammatory changes about the bile passages and bile thrombi⁷ within the lumen of the canaliculi apparently were the cause of obstructive jaundice.

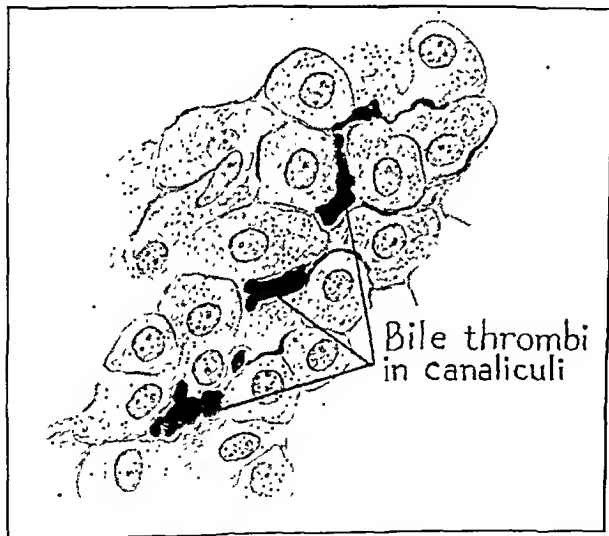


Fig. 3 (case 2).—Drawing of a high power field showing bile capillaries distended with bile thrombi.

These are not the usual features of arsphenamine hepatitis as reported in the literature or as observed at the Presbyterian Hospital. The histologic picture has been described, however, in association with non-

arsphenamine jaundice,⁸ as "cholangiolie" by Naunyn,⁹ "primary intrahepatic cholangitis" by Siegmund¹⁰ and by Eppinger as a "periacinar or cholangitic form of catarrhal jaundice."¹¹ Pericholangitis unassociated with disease of the extrahepatic biliary tract is probably not rare,⁸ but marked lesions were found only twelve times

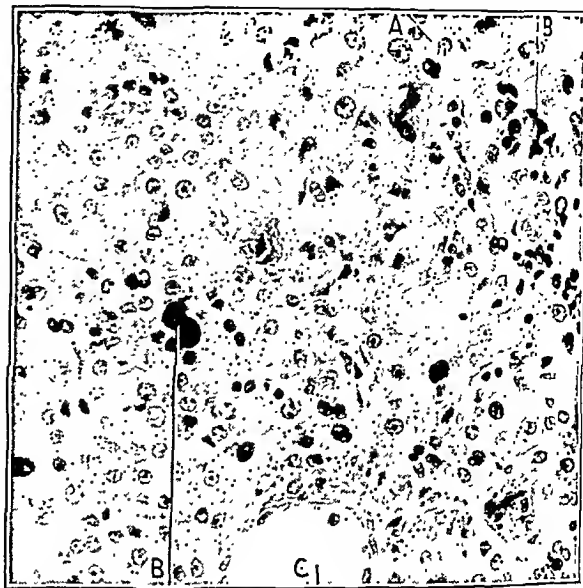


Fig. 4 (case 7).—Section of central portion of a liver lobule showing bile plugs in small biliary radicles. The Kupffer cells are mottled with bile pigment. A, bile in canaliculi; B, B, bile thrombi; C, central vein.

in 3,500 autopsies at the Presbyterian Hospital, occurring usually with terminal infections or cachectic states. No bile plugs were noted in the canaliculi in these cases.

COMMENT

In the cases described here an obstructive type of jaundice developed early in the course of treatment with arsenicals. Some of the cases reported in the literature as "early" or "intertherapeutic" postarsphenamine jaundice (Irgang,¹² Genner¹³ and others) show the clinical features described in table 1, but we have been unable to find the obstructive type segregated as a distinct group. The cutaneous eruptions appearing in some of our patients were suggestive of "erythema of the ninth day," but jaundice is rarely associated with this condition.¹⁴ The early febrile onset suggests the hepatic Jarisch-Herxheimer phenomenon; however, the usual explanation for this reaction—reactivation of syphilis or liberation of spirochetal endotoxins—can hardly account for the appearance of icterus in case 7, in which there was probably no syphilis.

We are unable to estimate the incidence of the obstructive form of arsphenamine reaction. The twelve cases comprising table 1 are from the records of ninety-two patients with postarsphenamine jaundice admitted to the Presbyterian Hospital from 1930 to 1939. Less

8. Klemperer, Paul: Pathology of Icterus, New York State J. Med. 33: 1309 (Nov. 15) 1933.

9. Naunyn, Bernhard: Ueber Ikterus und seine Beziehungen zu den Cholangien, Mitt. a. d. Grenzgeb. d. Med. u. Chir. 31: 537, 1919.

10. Siegmund, Herbert: Selb. d. Cholangitis, Beitr. z. path. Anat. u. z. allg. Path. 37: 1, 1902.

11. Eppinger, Hans: Die Leber, Julius Springer, 1937.

12. Irgang, Samuel: The Problem of the Liver in Syphilis, Arch. Dermat. & Syph. 36: 1, 1935.

13. Genner, Viggo: By-Effects in connection with Special Reference to the Liver, Munksgaard, 1936.

14. Keim, H. L.: "Erythema of the Ninth Day" Following Administration of Arsphenamine, Arch. Dermat. & Syph. 31: 291, 1935. Robinson, S. S.: "Erythema of the Ninth Day" Complicated by Acute Hepatitis and Jaundice on Continuation of Arsphenamine Therapy, ibid. 37: 1031 (March) 1938.

6. Dr. Theodore Rosenthal and Dr. William Curth of the Bureau of Social Hygiene, New York City, made this case available.

7. Hans Eppinger (Beiträge zur normalen und pathologischen Histologie der menschlichen Gallencapillaren mit besonderer Berücksichtigung der Pathogenese des Ikterus, Beitr. z. path. Anat. u. z. allg. Path. 31: 230, 1902) and others have produced similar bile thrombi experimentally and believe that they are formed by the outpouring of coagulable protein into the injured ducts.

severe forms of the reaction, with transient icterus not requiring hospitalization, doubtless occur. Mixed forms with concurrent parenchymal involvement, as indicated by a positive cephalin flocculation test, may also be encountered (case 10).

The nature of the toxic manifestations shown by the patients in table 1 is a matter of speculation. It seems unlikely from the evidence at hand that hepatic syphilis, arsphenamine overdosage and intercurrent "catarrhal" jaundice are important etiologic factors. The general pattern of the reaction has many of the characteristics of drug hypersensitiveness: 1. The initial injection of arsphenamine was without incident, but symptoms were precipitated by a second or third injection after a latent period. 2. The reaction was induced by relatively small amounts of arsenic. 3. In many cases there were associated cutaneous rashes, arthralgias, edema, eosinophilia and the like. 4. Further injections of arsenicals provoked more rapid and more severe recurrences of symptoms. It is known that after injection colloidal arsphenamine is rapidly stored in the Kupffer cells of the liver and other parts of the reticulo-endothelial system where degradation products are slowly formed. The original substance is relatively nontoxic to liver parenchyma, and the hepatic degeneration characterizing post-arsphenamine hepatitis is usually attributed to diffusible derivatives.¹³ Since parenchymal lesions are not striking in our cases it seems probable that the selective involvement of the finer biliary radicles represents a different type of toxic reaction induced in predisposed individuals by the freshly injected drug in colloidal form.^{14a}

Selective injury of the finer biliary radicles, which is so striking in the liver biopsies of the arsphenamine cases described, may be produced by a number of toxic agents.⁹ It has been observed in experimental toluylene-diamine poisoning, a condition found by Bodansky¹⁵ to be associated with unusually high serum phosphatase and cholesterol values. Dinitrophenol may also cause jaundice with clinical, chemical and pathologic features of intrahepatic biliary obstruction. We have recently observed such a case in which liver biopsy disclosed pericholangitis following the use of this drug as an anti-obesic. Eppinger¹¹ has noted similar lesions in the liver in occasional cases of "catarrhal" jaundice of undetermined etiology and has pointed out the difficulties in distinguishing this group from cases of extrahepatic biliary obstruction.

TREATMENT

The recognition of the obstructive type of reaction is of some practical importance in the management of post-arsphenamine jaundice. The administration of arsphenamine in these cases should be interrupted, perhaps discontinued. Although patients with some "early" types tolerate continuation of the drug, all of our patients reacted unfavorably when therapy was maintained.

The condition may be confused with obstruction of the extrahepatic biliary tract, and exploration may be performed for suspected common duct occlusion. No obstruction was found in our cases, but it is of interest that in case 2 noteworthy improvement followed cholecystectomy and liver biopsy. The therapy in these obstructive cases should be directed toward promoting drainage of the biliary tract rather than toward the con-

servation of injured liver parenchyma. Frequent large intravenous hypertonic dextrose infusions and choleric agents, such as bile salt preparations, or cholic acid derivatives¹⁶ should be given as early as possible after the appearance of jaundice.

SUMMARY

In twelve cases of postarsphenamine jaundice icterus was not of the usual hepatogenous type but appeared to be due to obstruction of the intrahepatic biliary tract. The clinical, chemical and pathologic features of this group suggest a distinct type of reaction to intravenous arsenicals characterized by:

1. Acute onset with constitutional and gastrointestinal symptoms coming on several hours after the second or third intravenous arsenical injection.
2. Appearance within several days of jaundice which may persist for weeks or months unaccompanied by other symptoms except pruritus.
3. Indications by various laboratory criteria of obstructive jaundice with little or no evidence of liver cell degeneration.
4. Preservation of essentially normal parenchyma in liver biopsies, the principal lesion being pericholangitis and bile thrombi in the finer biliary radicles.
5. Eventual recovery of the patient.

RANGE OF NORMAL BLOOD PRESSURE AND SUBSEQUENT DEVELOPMENT OF HYPERTENSION

A FOLLOW-UP STUDY OF 1,522 PATIENTS

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It is now well established that the systemic blood pressure is variable and that it reacts to various forms of external and internal stimulation. Such fluctuations of the blood pressure have contributed to the difficulty in determining normal blood pressure. Robinson and Brucer¹ have emphasized the difference of opinion as to what is normal blood pressure and have attempted in an extensive statistical study to determine more exactly the range of normal blood pressure. I have thought that if the range of variability of the blood pressure should be considered in addition to the level of blood pressure of any moment, some of the difficulties of determining whether or not an individual had normal blood pressure would be obviated. To use this conception, criteria for the normal range of blood pressure must be established. Some progress has been made regarding this through the use of standard tests for measuring the variability of the blood pressure (cold pressor test, breath-holding test) and by follow-up study of a group of subjects a number of years after the test was performed originally. The present study is an attempt to obtain further information about the normal range of blood pressure by determining the significance of elevation of the blood pressure in the upper ranges of normal as the result of the stimulus of a physical examination (nervous stress).

It has been the custom to regard transient elevations of blood pressure as of little significance. In fact some

14a. Biedermann, A.; Hanssen, E., and Wright, H. N.: Relation Between Colloidal Properties and Toxicity of Arsphenamine and Neo-arsphenamine, *Proc. Soc. Exper. Biol. & Med.* 31:172 (Nov.) 1933.
15. Bodansky, Aaron: Non-Osseous Origins of Serum Phosphatase: The Liver, *Enzymologia* 3:258, 1937.

16. Appel, Bernard, and Jankelson, I. R.: Treatment of Arsenical Hepatitis with Sodium Dehydrocholate: Experimental and Clinical Studies in Cases of Arsphenamine Poisoning, *Arch. Dermat. & Syph.* 32:422 (Sept.) 1935.

From the Division of Medicine, the Mayo Clinic.

1. Robinson, S. C., and Brucer, Marshall: Range of Normal Blood Pressure: A Statistical and Clinical Study of 11,383 Persons, *Arch. Int. Med.* 64:409-444 (Sept.) 1939.

physicians seem to think that, if one or several readings of blood pressure within the accepted normal range are obtained, the possibility of a patient's having hypertensive disease is excluded. In various textbooks and articles on blood pressure are statements to the effect that the patient should be in a comfortable position and mentally at rest when the blood pressure is taken so that readings indicative of any transient elevation of the blood pressure may be avoided. My experience with the cold pressor test has led me to believe that

TABLE 1.—Incidence of Subsequent Hypertension According to Original Systolic Blood Pressure

Original Reading of Systolic Blood Pressure, Mm. of Mercury	10 Year Group			20 Year Group		
	Subsequent Hypertension			Subsequent Hypertension		
	Cases	Cases	Per Cent	Cases	Cases	Per Cent
Below 110.....	76	0	0	77	0	0
110-119.....	194	4	2.1	184	9	4.9
120-129.....	212	13	6.1	230	30	12.6
130-139.....	103	11	10.7	142	48	33.8
140-149.....	86	34	39.5	111	70	63.1
150-160.....	61	37	60.7	37	29	78.4
Total.....	732	99	13.5	700	186	23.5

any transient elevation of the systolic and diastolic blood pressure above a certain level should be regarded as evidence of a hyperreactive regulating mechanism for blood pressure and that in many instances this hyperreactivity is a precursor of sustained hypertension.

Previous studies concerning the significance of elevation of the blood pressure to the upper ranges of normal have consisted almost exclusively of analysis of insurance data in which the incidence of mortality has been used to determine the significance of different levels of high "normal" blood pressure. This method is open to obvious objection if an attempt is being made to determine the significance of an elevated blood pressure as to the probability of the development of subsequent hypertension. There has been no follow-up study of a large group of persons after a long period in which readings of blood pressure and examinations of the ocular fundi were used to indicate subsequent hypertension.

Diehl and Hesdorffer² have follow-up data on 155 students for seven years and they concluded that "young men who show persistent, intermittent or even transient elevations of blood pressure during their college years are much more likely to have elevated pressures after a period of from five to ten years than those in whom the blood pressure was consistently normal while they were in college." Palmer³ studied the records of 3,598 routine physical examinations in the department of hygiene at Harvard University. He found a systolic blood pressure of more than 140 mm. of mercury in 10 per cent and of more than 150 mm. in 2 per cent. He obtained follow-up data after ten years on forty-nine of the persons with elevated blood pressure and sixty-six without elevated blood pressure and found that only 4.5 per cent of the latter had blood pressure of more than 140 mm., whereas 22.5 per cent of the group whose blood pressure was elevated originally had hypertension. He concluded that "if hypertension is found at 20 years of age it is somewhat more likely to be found persistent after ten years than it is to develop *de novo* during this interval."

As previously mentioned, Robinson and Brucer have made a detailed statistical study of the blood pressure of a large group of persons. They have concluded that the normal range of systolic blood pressure is between 90 and 120 mm. of mercury and that the normal range of diastolic blood pressure is between 60 and 80 mm. They probably have given a reliable estimation of the range of normal blood pressure under resting conditions, but their data will not indicate the possible significance of transient elevations of blood pressure of subjects whose blood pressure is usually normal, as they state "In all cases of abnormally high or low readings a reading was repeated as a check at the end of the examination to discount emotional or transitory rises, the lowest readings being recorded."

BASIS OF PRESENT STUDY

I noted that in many instances there was a correlation between the "ceiling," or maximal response, of the blood pressure of a patient to the cold pressor test and the first reading of the blood pressure taken on the same patient in the office at the clinic.⁴ This correlation was noted also by Ayman and Goldshine⁵ in their work with the cold pressor test. The first reading of blood pressure at the Mayo Clinic generally is taken by a physician with whom the patient is unacquainted and in strange surroundings. Consequently the first reading of the patient's blood pressure represents that individual's vasomotor reaction to nervous tension, which is in effect a psychic pressor test. This type of reaction is not as consistent as the response to a standard test like the cold pressor test, but it is sufficiently constant for the purposes of this study. Records of patients who have returned many years after their first examination at the Mayo Clinic are available in the files. By studying these records, it should be possible to determine whether or not hyperreactivity of the blood pressure to nervous stress is indicative of a prehypertensive phase

TABLE 2.—Incidence of Subsequent Hypertension According to Original Diastolic Blood Pressure

	10 Year Group			20 Year Group		
	Subsequent Hypertension			Subsequent Hypertension		
	Cases	Cases	Per Cent	Cases	Cases	Per Cent
Below 70.....	88	0	0	110	0	0
70 - 74.....	146	5	3.4	144	2	1.4
75 - 79.....	83	2	2.4	83	4	4.8
80 - 84.....	225	5	2.2	187	13	7.0
85 - 89.....	48	12	25.0	110	63	57.3
90 - 94.....	85	35	41.2	103	67	65.0
95 - 100.....	57	40	70.2	43	37	86.0
Total.....	732	99	13.5	700	186	23.5

of essential hypertension. Furthermore, such data should give some indication of the prognostic significance of a borderline reading of blood pressure.

This study is based on review of the records in 1,522 cases. Two groups of cases were selected. In one group the patients had returned to the clinic ten years and in the other twenty years after their first examination. On their first visit to the clinic, which occurred either in 1916 or in 1926, the initial reading of blood pressure of all these patients was less than 160 mm. of mercury systolic and 100 mm. diastolic. The initial reading of the majority of patients was within the com-

2. Diehl, H. S., and Hesdorffer, M. B.: Changes in Blood Pressure of Young Men Over Seven Year Period, *Arch. Int. Med.* 52: 948-953 (Dec.) 1933.

3. Palmer, R. S.: The Significance of Essential Hypertension in Young Male Adults, *J. A. M. A.* 94: 694-697 (March 8) 1930.

4. Hines, E. A., Jr.: The Significance of Vascular Hyperreaction as Measured by the Cold Pressor Test, *Am. Heart J.* 19: 408-416 (April) 1940.

5. Ayman, David, and Goldshine, A. D.: Cold as a Standard Stimulus of Blood Pressure: A Study of Normal and Hypertensive Subjects, *New England J. Med.* 219: 650-655 (Oct. 27) 1938.

monly accepted normal limits, for only 4.4 per cent had blood pressure readings on the first visit of more than 145 mm. systolic and 90 mm. diastolic. None of them gave a history of previous hypertension or had pathologic conditions which might be said to have produced hypertension at the time or later, such as hyperthyroidism, toxemia of pregnancy or any renal or vascular disease.

The conclusions from this study are based on a comparison of the original reading of blood pressure

TABLE 3.—*The Incidence of Subsequent Hypertension According to Original Blood Pressure*

Original Blood Pressure, Mm. of Mercury		10 Year Group			20 Year Group		
		Subsequent Hypertension		Cases	Subsequent Hypertension		Cases
Systolic	Diastolic	Cases	Per Cent		Cases	Per Cent	
Below 140	Below 85	514	12	2.3	506	19	3.8
Above 140	Below 85	28	0	0.0	28	0	0.0
Below 140	Above 85	71	17	23.9	136	68	50.0
Above 140	Above 85	119	71	59.7	120	99	82.5
Total.....		732	99	13.5	790	186	23.5

as recorded on the first visit to the clinic and the presence or absence of hypertension when the patients were reexamined ten or twenty years later. The term "subsequent hypertension" as used in this paper implies one or several readings of blood pressure obtained at the time of the last visit in which the systolic blood pressure was more than 160 mm. and the diastolic more than 100 mm. In the majority of cases there was additional evidence of hypertension in the ocular fundi. This criterion is subject to some objection as it arbitrarily eliminated a few patients with a subsequent systolic reading of less than 160 mm. who definitely had hypertensive disease, as shown by evidence in the ocular fundi and by a diastolic reading of more than 100 mm. However, this group is so small that its inclusion among the group without subsequent hypertension has not materially affected the results.

SUMMARY OF DATA

Of a total of 1,522 patients 614, or 40.3 per cent, were men and 908, or 59.7 per cent, were women. The average age of the women at the time of their first visit was 35.5 years and of the men 39.1 years.

The incidence of subsequent hypertension according to the original systolic and diastolic readings is given in tables 1 and 2. It will be noted that the higher the original reading of blood pressure the higher the incidence of subsequent hypertension. The small incidence of subsequent hypertension when the diastolic reading was less than 85 mm. at the time of the first admission is particularly striking. The incidence of subsequent hypertension when both the systolic and the diastolic readings at the first admission were considered is shown in table 3. When both the systolic and the diastolic readings were elevated, the incidence of subsequent hypertension was very great. Even when the systolic blood pressure was less than 140 mm., if the diastolic blood pressure was more than 85 mm. the incidence of subsequent hypertension was high. It is of particular interest that in the group of patients who had systolic blood pressure of more than 140 mm. but diastolic blood pressure of less than 85 mm. none had subsequent hypertension.

An analysis of the effect of age on the subsequent development of hypertension reveals that, if the blood pressure is elevated into the upper range of normal at

the time of the original visit, the greater the age at that time, the greater will be the incidence of subsequent hypertension (table 4). However, in any given age group the general trend is for the development of subsequent hypertension among these patients who had a high normal blood pressure and for absence of subsequent hypertension among those who had low normal blood pressure. A more detailed statistical analysis of the effect of age on the blood pressure in this group is being carried out and will be reported at a later date.

Of the patients who were 50 years of age or more when the original reading of blood pressure was taken, seventy-three had hypertension ten or twenty years later. This does not support the idea that if a person is to have hypertension he necessarily should have it by the time he is 50 years of age.

The ocular fundi of 159 patients were examined at the time of the original visit. One hundred and thirty-one of the patients did not have hypertensive changes in the ocular fundi and in fourteen, or 11 per cent of these, hypertension developed subsequently. Twenty-eight had hypertensive changes, of grade 1 or 1+ in almost every instance, and in twenty-two, or approximately 80 per cent of these, hypertension developed subsequently.

That the group of patients with subsequent hypertension had a significant degree of hypertension is indicated by the fact that the mean blood pressure at the last examination for this group was 185 mm. systolic and 110 mm. diastolic. The systolic blood pressure of approximately 80 per cent was more than 170 mm. and of 38 per cent more than 190 mm. The diastolic reading of approximately 65 per cent was more than 110 mm. Approximately 70 per cent of the group with subsequent hypertension had examinations of the ocular fundi at the last examination; of these, 2 per cent had changes of group 4, 19 per cent changes of

TABLE 4.—*Incidence of Subsequent Hypertension Among Patients Who Had a High Normal Blood Pressure **

Age, Years at Original Visit	10 Year Group			20 Year Group		
	Subsequent Hypertension		Patients	Subsequent Hypertension		Patients
	Number	Per Cent		Number	Per Cent	
10-19	0	0.0	0	2	2	100.0
20-29	5	3	60.0	19	11	57.9
30-39	22	9	40.9	35	29	82.9
40-49	51	34	66.7	42	25	81.3
50-59	32	17	53.1	19	19	100.0
60-69	8	7	87.8	3	3	100.0
70-79	1	1	100.0	0	0	0.0
Total	119	71	59.7	120	99	82.5

* Original blood pressure between 140/85 and 160/100.

group 3, 43 per cent changes of group 2 and 36 per cent changes of group 1. The changes in the ocular fundi were those seen in Keith and Wagener's classification of hypertension groups 1 to 4.

SUMMARY

The records of 1,522 patients who returned to the clinic ten or twenty years after an original visit have been reviewed. An analysis has been made of the incidence of subsequent hypertension as correlated with the first reading of blood pressure recorded on the original visit. This first reading of blood pressure is thought to represent, in most instances, a response of blood pressure to nervous stress.

The results of this study support the idea that excessive variability or excessive responses of the usually

normal blood pressure to stimulation should be considered as evidence of a possible prehypertensive state. The range of normal blood pressure has not been definitely established by this study. However, patients whose blood pressures are not elevated, as a result of nervous stress, to more than 140 mm. of mercury systolic and (or) 85 mm. diastolic are unlikely to develop hypertension subsequently. If the blood pressure under such circumstances is less than 120 mm. systolic and 70 mm. diastolic, the patient is almost certain not to have hypertension subsequently. Conversely, even transient elevations of the systolic and diastolic blood pressures into the upper ranges of normal are prognostic of probable subsequent hypertension. Elevation of the systolic blood pressure alone is not indicative of subsequent hypertension. In this group of patients, 85 mm. marked a critical level of the diastolic pressure as to the possible occurrence of subsequent hypertension. It is recognized in this study that age is a factor in the incidence of subsequent hypertension; however, in general the results of this study hold true regardless of the age of the patient.

SELF-SELECTED DIETS IN TOXIC GOITER

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Normal limits of any physiologic factor are established from averages of measurements on normal subjects. For example, in determining the normal height of an individual at any given age the height values of normal persons of that age are averaged and tabulated. The same is true for determinations of normal weight or the normal metabolic rate and other measurements at various ages.

Following the same procedure it should be possible to establish the normal in diet by analyzing food mixtures representing self-selected diets consumed over, say, a three day period, using for this study persons of presumably normal health. By including in such studies individuals of different ages and occupations of normal life expectancy and reproductive capacities, it should be possible to determine if there is such a thing as a normal diet. In other words, do normal individuals living continuously in a state of good health instinctively select a diet containing proteins, fats and carbohydrates in percentages fairly constant in amount, or falling within narrow limits of percentage variations, to form what could be called a normal diet?

It would be difficult indeed to demonstrate that a diet established as normal by this method is injurious to a normal person. Certainly it is much easier to prove that various diseases and vague states of ill health develop among those who have been led or forced to adopt diets differing essentially from such an average, or normal, diet.

Where foods are available in normal variety and amount it appears that the instinctive control of food intake by the normal hunger sense is capable within wide limits of maintaining the individual in health for the average span of life. Nor does this instinctive control seem to be superior in animals or in savages whose dietary habits have been studied when compared with that of civilized man.

Despite changes caused by modern methods of food distribution and preparation, man still retains his ability

to adapt himself to these changes. Instinct, however, is not an infallible guide and fails to ward off deficiency diseases, many of which become evident only after prolonged use of a diet lacking in certain necessary constituents.

How far, therefore, can one's hunger sense be trusted in the self selection of diet?

In testing the ability of rats and mice to choose between adequate and inadequate diets, Mitchell and Mendel¹ concluded that their results are in harmony with the conclusions earlier expressed by Osborne and Mendel that "the desire of a young animal for food is something more than the mere satisfaction of calorific needs. The demand made by the growth impulse must be met by a food of the proper chemical constitution."

Evvard² states that when the appetite is given full control of what shall be eaten it is surprising to note how pigs naturally select the food combination which swine herdsman have long since approved of as the best and show a marked avoidance of those foods usually considered as ill adapted to swine.

Hutchinson³ believes that the appetite of the growing child is far more reliable than the nutritional standards of either mother or physician.

Davis⁴ reports experimental studies on self-selected feeding of newly weaned infants. Analyses of the foods were not made, but examination of their food records showed that in spite of the apparently chaotic manner of selection, their intakes of protein, carbohydrate and fat bore an orderly relation to each other and did not differ widely in the group.

On the basis of the average composition of 134,879 rations issued in 427 messes in different army camps, Murlin and Hildebrandt⁵ report the average food consumption per man per day. In their investigation analysis of the food itself was made. They found that the food constituents averaged 14 calories of protein, 31 calories of fat and 55 calories of carbohydrates to every hundred calories of food ingested, i. e., on a percentage basis the food ingested was analyzed as 14 per cent protein calories, 31 per cent fat calories and 55 per cent carbohydrate calories.

Voit⁶ gives the following ration for the use of a man at average hard labor: 16 per cent protein calories, 67 per cent carbohydrate calories and 17 per cent fat calories, the diet to contain 3,055 calories daily. For a man at hard work he allows 17 per cent protein calories, 58 per cent carbohydrate calories and 26 per cent fat calories in a diet containing 3,574 calories daily.

Lavonius⁷ relates that champion wrestlers during their periods of effort ingest 18 per cent protein calories, 35 per cent carbohydrate calories and 47 per cent fat calories for a total of 5,070 calories daily. In another instance he found 18 per cent protein calories, 38 per cent carbohydrate calories and 44 per cent fat calories for a total of 4,254 calories daily.

Sundstrom⁸ states that the diet of the average farmer of Finland contains 15 per cent protein calories, 64 per

1. Mitchell, H. S., and Mendel, L. B.: *Am. J. Physiol.* 58:211 (Dec.) 1921.

2. Evvard, J. M.: *Proc. Iowa Acad. Sc.* 22:400, 1915.

3. Hutchinson, Woods: *We and Our Children*, New York, Doubleday, Page & Co., 1911.

4. Davis, Clara M.: *A Practical Application of Some Lessons of the Self-Selection of Diet Study to the Feeding of Children in Hospitals*, *Am. J. Dis. Child.* 46:743 (Oct.) 1933; *J. Am. Dent. A.* 21:636 (April) 1934.

5. Murlin, J. R., and Hildebrandt, F. M.: *Am. J. Physiol.* 40:531 (Sept.) 1919.

6. von Voit, C., in Hermann, L.: *Handbuch der Physiologie*, Leipzig, F. C. W. Vogel, 1881, vol. 6, pt. 1, p. 519.

7. Lavonius, H.: *Skandinav. Arch. f. Physiol.* 17:196, 1905.

8. Sundstrom, S.: *Untersuchungen über die Ernährung der Landbevölkerung in Finnland*, Helsingfors, 1908.

cent carbohydrate calories and 21 per cent fat calories in a total of 3,474 calories daily.

Pepe and Perelli⁹ give a table showing the items composing the diets fed in a boys' colony which contained 16 per cent protein calories, 70 per cent carbohydrate calories and 10 per cent fat calories, and the diets fed in a girls' colony containing 15 per cent protein calories, 73 per cent carbohydrate calories and 8 per cent fat calories. These subjects were about 9 years old. The average daily number of calories for the boys was 2,212 and for the girls 1,827.

Mary Rose¹⁰ gives a table to show distribution of calories as estimated by Professor Krogh, of the University of Copenhagen, for three types of diet, with high, medium, and low proportions of protein.

Here it is obvious that the protein content of the Eskimo diet is abnormally high simply because the diet of the Eskimo is not really self selected but is merely the only diet available to him. The same may be said of the low protein content of the diet of the Bengali. Indeed, the only apparent reason for the wide variations in percentage distribution seen in the diets of these and numerous other groups as presented in reports of similar kind is that the diets analyzed were imposed on the subject or were self selected only in a limited sense.

In reporting this study of the self-selected diets of persons of various ages and occupations attention is called to a noteworthy fact revealed by repeat or follow-up tests in any given case. These repeat tests have consistently shown that, within reasonably narrow limits of variation, the percentage of protein calories in the self-selected diet of a given subject is characteristic of the individual.

On the basis of caloric percentage (not grams per day), a given proportion of protein calories in the calories of the diet is habitually selected by one individual, while an entirely different percentage is quite as habitually preferred by another—provided, of course, that the subject is in physiologic balance.

The personal preference displayed by each is relatively constant and therefore dependable as a basis for classifying individuals in accordance with the data here

TABLE 1.—Distribution of Calories in Typical Diets						
Type of Diet	Weight, Kg.	Protein, Gm.	Total Calories	Distribution of Calories, %		
				Protein	Fat	Carbohy- drate
Eskimo.....	65	282	2,604	44	48	8
Bengali.....	50	52	2,379	9	10	81
European.....	70	118	3,055	16	17	67

reported. A very practical proof that it is constant is the fact that dietary habits may be redirected or changed only with difficulty and considerable perseverance, as those who have attempted to treat ailments due to dietary imbalances will agree.

One individual in this series, whose diet was analyzed in three day specimens on fourteen separate occasions at varying intervals over a four year period, showed a maximum of 13.2 and a minimum of 12.5 per cent protein calories, or an average variation of less than 0.4 per cent of the total calories. This record was achieved with no conscious attempt on the part of the subject to maintain regularity in the selection of food, either in kind or in amount.

Analyses of food requirements of large groups of persons in health, as reported by other workers, very well show the average, or normal, percentage distribution of calories; but it is obvious that analyses of individual diets would be required to show if self-selected diets under some conditions tend to become unbalanced, and whether or not accurate measurements of such dietary imbalances have diagnostic value.

The purpose in presenting this paper, therefore, is to outline briefly the routine used in studying the dietary habits of individuals rather than groups, to determine whether or not any given deviation from the normal

TABLE 2.—Method of Recording Experimental Data			
	Grams per Hour	Calories per Hour	Percentage of Total Calories
Urinary nitrogen.....	0.600
Dietary nitrogen.....	0.680
Protein.....	4.27	17.5	13.1
Fats.....	5.25	48.8	36.4
Carbohydrates.....	16.50	67.6	50.5
Salts.....	0.53
Total solids.....	23.55	133.9

diet is constantly associated with any group of symptoms, vague states of ill health or diseases of unknown origin.

One very practical application in connection with individual analyses of self-selected diets has already developed as a result of this method of approach. Preliminary data on that work are also included in this report.

COLLECTING THE FOOD AND URINE SPECIMENS

Each experiment was extended over a three day period. This tended to smooth out any irregularities in food intake and urinary nitrogen output, which often occur in shorter periods owing to variations in appetite or eating habits from day to day.

For obvious reasons it is necessary to employ only those subjects who, as determined by inquiry and checked by weighing at the beginning and end of the three day dietary experiment, show no recent consistent loss or gain in body weight.

Analysis of the self-selected diet begins with questioning the patient in detail and recording all answers regarding his eating habits. He is closely questioned concerning each meal of the day, as to what he eats, how much, or what size portions, how many times a week, how often he changes to a different type of meal, and what, how much and how often he takes of food or drinks between meals. This record of his own statement is filed for future use in checking against the food he brings in later.

The subject is then directed to maintain the same dietary habits and to refrain from any exercise, such as spring cleaning or gardening, not of his regular daily routine during the three day collection of the self-selected diet. He is provided with bottles to save all fluid foods separately—milk in one bottle, fruit juice in another, carbonated drinks in another, and so on. These have labels attached for recording separate daily amounts, to account for the three day total of each as they are accumulated for analysis. Fruit jars are used for saving moist foods, with labels attached for recording the meal and date. Dry foods are brought in wrapped, labeled and dated parcels.

Because the method of analysis requires drying to constant weight and because the protein content of alcoholic drinks is nil, these are not brought in but are

9. Pepe, M., and Perelli, S.: Quaderni di nutrizione 4:327, 1937.
10. Rose, Mary S.: Foundations of Nutrition, ed. 3, New York, The Macmillan Company, 1938.

recorded and their caloric content is then estimated if they regularly make up any appreciable percentage of the diet. Coffee and tea drinks are not saved, but only the sugar and cream used in them.

Weighing the food to secure accurate duplicate portions interferes with spontaneous appetite and is therefore a handicap.

With subjects of even moderate intelligence it is also unnecessary. The object in using the patient's food portions is not so much to duplicate the exact number of calories as it is to determine the percentage distribution of the calories. In other words, an error of a few grams in the weighing of any given serving of food affects the total of

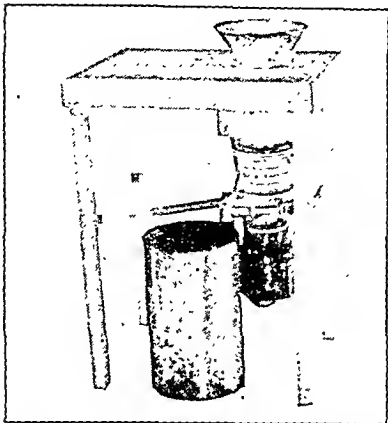


Fig. 1.—Electric food grinder (mounted through table top) for reducing food specimen to consistency of peanut butter.

calories but does not appreciably affect the proportions of the protein, fat and carbohydrate calories in the final three day total of food.

As the subject serves himself he serves a similar portion into the food container, removing bones, gristle, fat, peelings or other inedible parts, exactly as he does from the portions he eats. If the subject fails to eat all of any serving, obviously a similar amount is removed from the portion to be put into the food container.

The food, when brought in these containers and kept separately, as directed, is in suitable condition to be inspected for the obvious purpose of determining whether it corresponds to the subject's own description

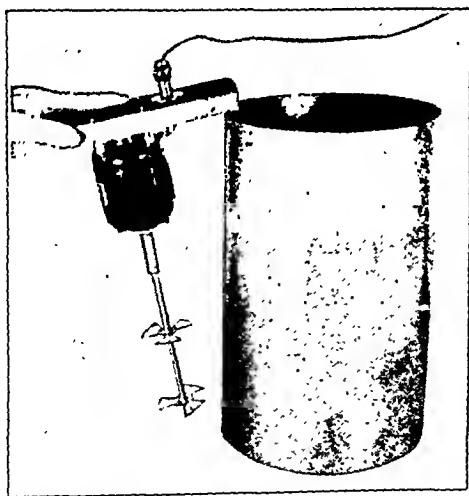


Fig. 2.—Electric stirrer and stirring vessel. For obtaining accurate duplicate checks, sampling must be done while food mass is kept in homogeneous state by rapid stirring.

of his diet. The food portions as they accumulate are kept under refrigeration to protect against fermentation.

The subject is also asked to save all metabolized nitrogen (urine) passed during this period, the total urinary nitrogen serving as a check on the food nitrogen, since approximately 90 per cent of the food nitrogen is metabolized and then recovered in the urine.

Thus, when the nitrogen recovered in the urine fails to equal approximately 90 per cent of the nitrogen found in the food specimen, the experimenter may know that (1) not all of the urine was saved, (2) servings of food were not duplicated, or (3) the subject either lost or gained weight during the three day period. It should be determined which of these possibilities actually occurred.

Rarely will patients deliberately deceive in saving the specimens of urine and food. They merely require instruction. When the routine and purpose are carefully explained to them repeat tests are not required more often than in any other form of quantitative studies.

The urine specimens are collected in gallon bottles and preserved against ammoniacal fermentation (loss of nitrogen) by the use of 15 Gm. of tartaric acid. A quart bottle collapsing into a close-fitting metallic or nonbreakable pitcher, the latter, in turn, closely fitting into a small case with a handle similar to the ordinary size compact, is provided for those obliged to be away from home during the three day period, as for work or for social engagements.

ANALYZING THE URINE

Many modifications of the regular Kjeldahl method (nesslerization and other methods) for determining total urinary nitrogen have proved unsatisfactory and should

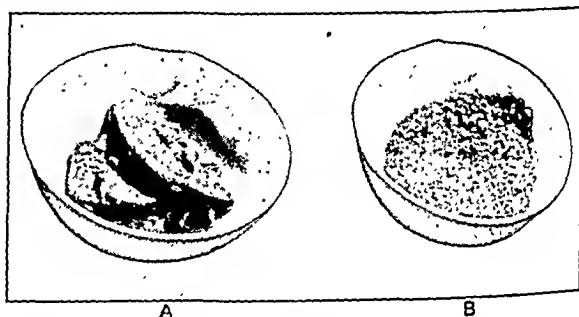


Fig. 3.—One hour's food portion: A, after grinding and drying to constant weight; B, after grinding by mortar and pestle, to obtain aliquot part for protein and fat determinations.

not be used. The allowable error here should not exceed 1 per cent. The original Kjeldahl routine giving this required accuracy may be found in any accepted laboratory manual.

The nitrogen is computed on the basis that each cubic centimeter of tenth-normal acid neutralized by the ammonia distilled over is equal to 1.4 mg. of nitrogen in the 5 cc. of the mixed urine used in the analysis. Since the total seventy-two hour urinary volume is known, the number of milligrams of nitrogen per hour is easily calculated. The amount is then compared or checked against that found in the food specimen, to be analyzed as follows:

ANALYZING THE FOOD SPECIMEN

The entire seventy-two hour specimen of solid and liquid foods is put through a food grinder for reduction to peanut butter consistency. The mass as it comes from the grinder (fig. 1) is allowed to fall directly into a stirring vessel (fig. 2) of approximately 15 liter capacity and of known empty weight, which should be about 5 to 10 pounds (2 to 4 Kg.).

Ordinary tap water heated to 50 C. is used to wash into the stirring vessel all food adhering to the grinder. Then the same hot water is added until the mixture causes the vessel to weigh 10,080 Gm. more than its known empty weight.

n for using hot water is

that it keeps the fats from separating out until duplicate specimens for analyzing have been secured.

The hot watery material is now stirred by an ordinary electric stirrer (fig. 2) until the entire mass is thoroughly mixed. Specimens for analysis are removed in duplicate and only while the mixture is being thoroughly stirred. Scales sensitive to within about 20 mg. at a 500 Gm. load are used for weighing the specimens to be analyzed. The total weight of the seventy-two hour mixture was purposely made 10,080 Gm. so that $\frac{1}{2}$ of it, or a one hour food portion, would weigh $\frac{1}{2}$ of 10,080 Gm., or 140 Gm. This 140 Gm. specimen is of convenient size for analysis and gives results directly in terms of units per hour, as in common use in metabolic studies. The 140 Gm. samples are weighed in flat bottom dishes of about 4 inch (10 cm.) diameter so as to facilitate evaporating the water later. To secure homogeneous and accurate duplicates, when dipping out these samples one uses a 300 cc. beaker, immersing it directly into the stirring mass.

As the mass is being poured into the flat bottom dishes for weighing the 140 Gm. samples, the watery mixture in the beaker is kept constantly stirred by spoon until the 140 Gm. tilts the scales. If more than 140 Gm. is inadvertently poured into the dish, the excess should not be removed without stirring the dish. When not so stirred with each removal to or from the sample during weighing, a portion taken from the top will be watery, or from the bottom will be more concentrated with solids, from rapid settling, and this will result in error due to sampling.

As an extra precaution, about 1 liter of the stirred seventy-two hour specimen is removed to a wide mouth, serew cap jar and kept in reserve in the ice box for emergency, against a need for repeat analysis.

The duplicate 140 Gm. samples are kept in a drying oven at 70 C. for forty-eight hours. The solids, ranging from 10 to 35 Gm., should check within less than 1 per cent in the duplicates. After removal from the dish and grinding by mortar and pestle a granular product is obtained; this is remarkable in its similarity to other specimens in all types of cases and in its close resemblance to grape-nuts in consistency, color, odor and taste (fig. 3).

An aliquot part, a convenient, 10 Gm. quantity, is used for extracting the fat with ether by the Soxhlet apparatus. Similarly, an accurately weighed 1 Gm. portion of the sample is used for total nitrogen determination by the method used for analyzing the urine, except that 4 drops of a saturated solution of copper sulfate is added to hasten the oxidation by sulfuric acid and the additional food materials are subjected to continuous heating for from one and one-half to two hours, or until the blackened mixture becomes only slightly straw colored.

By calculation the grams per hour of fat (Soxhlet extraction) and grams per hour of protein (Kjeldahl) in the one hour's portion of food may thus be determined. The weight of the total solids minus the combined fat and protein weights gives the weight of the carbohydrates and salt. (Fibrous vegetables and other residue, when thus dried to constant weight, form an unimportant fraction of the total solids of the sample).¹¹ Salt content is approximated as 2 per cent of the total dried mass, so that the latter, minus the weight of the proteins, fats and salts, gives the weight of the carbo-

hydrates. Table 2 illustrates the method of recording the essential data and computation of the percentage distribution of protein, fat and carbohydrate calories.

The figures in table 3 showing the percentage distribution of calories in normal subjects are in good agreement with the averages of those who have reported analyses of the diets of groups of normal, active persons. The averages for the group, 14.4 per cent protein, 34.7 per cent fats and 50.6 per cent carbohydrates, do not vary appreciably from the group averages reported by Murlin and Hildebrandt to which reference was made

TABLE 3.—Distribution of Calories in the Diet of Normal Subjects

Case	Subject	Occupation	Sex	Age	Percentage of Calories		
					Protein	Fat	Carbo- hydrate
1	C. A.	Carpenter.....	♂	28	15.0	38.2	46.8
2	B. A.	Bookkeeper.....	♂	30	14.9	37.7	47.4
3	M. A.	Housekeeper.....	♀	62	15.1	36.1	48.8
4	P. A.	Storekeeper.....	♂	37	15.0	35.0	50.0
5	J. J. B.	Chemist.....	♂	26	16.7	37.6	45.6
6	Bares	Salesman.....	♂	44	14.8	38.6	46.6
7	J. B.	Foundryman.....	♂	56	14.6	44.8	40.6
8	M. B.	Lawyer.....	♂	45	16.1	35.0	48.9
9	S. C.	Physician.....	♂	40	13.3	36.0	50.7
10	W. C.	Attorney.....	♂	61	13.0	37.2	49.8
11	M. C.	Typist.....	♂	20	14.9	37.5	47.6
12	D. C.	Mechanic.....	♂	20	14.0	39.6	45.4
13	W. C.	Gas station attend.	♂	23	15.5	35.8	48.7
14	J. C.	Salesman.....	♂	30	14.7	40.1	45.2
15	M. O.	Nurse.....	♀	30	14.3	36.2	49.5
16	A. D.	Mechanic.....	♂	16	15.0	29.6	55.4
17	H. D.	Typist.....	♂	23	15.4	31.0	53.6
18	R. D.	Mechanic.....	♂	16	14.3	32.7	53.0
19	T. D.	Mechanic.....	♂	16	13.4	35.2	51.4
20	E. D.	Machinist.....	♂	26	14.8	32.2	53.0
21	Dick	Machinist.....	♂	20	13.6	35.1	51.3
22	M. E.	Housemaid.....	♀	35	13.8	39.2	47.0
23	E-1	Physician.....	♂	26	13.5	35.9	50.6
24	E-2	Housekeeper.....	♀	36	13.7	37.2	49.1
25	E-3	Housekeeper.....	♀	26	14.3	31.1	54.6
26	E-4	Salesman.....	♂	27	13.1	32.0	56.9
27	E-5	Physician.....	♂	35	13.3	38.2	48.5
28	C. F.	Mechanic.....	♂	19	14.2	37.2	48.6
29	R. F.	Stenographer.....	♂	25	12.5	34.6	52.9
30	M. G.	Housekeeper.....	♀	30	13.8	36.9	47.3
31	B. G.	Housekeeper.....	♀	30	14.0	30.2	55.8
32	R. G.	Schoolboy.....	♂	17	14.0	39.1	46.9
33	A. D. H.	Chemist.....	♂	22	15.5	35.8	48.7
34	A. H.	Shipping clerk.....	♂	18	12.6	29.2	58.2
35	D. S. J.	Physician.....	♂	30	12.8	40.1	47.1
36	B. J. J.	Schoolgirl.....	♀	8	15.9	41.0	44.1
37	H. M. J.	Physician.....	♂	52	17.1	37.3	45.6
38	B. J.	Schoolboy.....	♂	14	15.6	37.8	46.6
39	J. K.	Housekeeper.....	♀	..	12.8	34.6	53.3
40	I. N.	Mechanic.....	♂	22	14.5	38.2	47.3
41	A. R. N.	Salesman.....	♂	37	12.8	35.3	52.0
42	N. A.	Housekeeper.....	♀	..	14.9	39.2	45.9
43	B. P.	Salesman.....	♂	32	15.5	36.0	48.5
44	T. P.	Housekeeper.....	♀	50	14.4	36.0	49.6
45	S. R.	Secretary.....	♀	..	13.0	39.2	47.8
46	L. S.	Technician.....	♂	20	14.9	35.1	50.0
47	P. S.	Storekeeper.....	♂	28	12.8	28.1	59.1
48	W. S.	Errand boy.....	♂	22	12.3	35.8	51.9
49	R. W.	Mechanic.....	♂	23	12.8	35.9	51.3
50	E. W.	Machinist.....	♂	23	15.5	32.3	48.5
Average.....					14.4	34.7	50.6

in a preceding paragraph. Individual variations from these averages are also without significance.

The beginning of this study was the observation that toxic goiter patients show a smaller urinary nitrogen output in proportion to their larger caloric intake than do normal subjects.

Naturally the suspicion arises at once that this smaller urinary nitrogen output per caloric intake is due to a protein deficiency in the diet of the toxic goiter patient. To demonstrate this protein deficiency in the diet it was necessary to make routine food analyses of the self-selected diets of toxic goiter patients showing varying degrees of thyroid enlargements, different types of goiters and all possible grades of toxicity.

For this study it was necessary to eliminate all goiter patients except those in whom all signs and symptoms necessary for an easy diagnosis of hyperthyroidism were present.

11. Atwater, W. O., and Woods, C. D.: The Chemical Composition of American Food Materials, Bulletin 28, United States Department of Agriculture, Office of Experiment Stations, 1896, p. 13.

Table 4 gives sufficient data to express the relative degree of toxicity together with the data obtained from analysis of the self-selected diet in each individual case. Comparing the normal series in table 3 with the toxic goiter series in table 4, it will be observed that no normal subject consumed as little as 12 per cent, whereas no goiter subject consumed as much as 12 per cent, of his calories as protein. In other words, owing to his high metabolism, the toxic goiter patient may consume more nitrogen per day, but the diagnostic point is that he consumes less nitrogen per calory than does the normal subject.

It may be argued that this preference for a diet low in protein is due to a craving for concentrated foods to maintain the increased metabolism. The difficulty with that explanation, however, is that even after thy-

the onset of goiter is, say, — 15 per cent in a given case, a beginning toxic goiter could cause the rate to increase several points and yet be found within normal limits at the time of examination, despite the beginning hyperthyroidism.

The clinical application of this relationship between protein dietary imbalance and toxic goiter is, therefore, its diagnostic use in cases characterized by marked fatigue, emotional instability and other symptoms of toxic goiter, but in which thyroid enlargement is doubtful and the basal metabolic rate is "normal." In every medical practice there is a high percentage of these cases showing all variations of this symptom complex. They have been variously diagnosed as hypochondria, autonomic imbalance, neurasthenia, effort syndrome and fatigue neurosis.

TABLE 4.—Distribution of Calories in the Diets of Hyperthyroid Patients

Case	Subject	Sex	Age	Basal Metabolic Rate, Plus	Signs and Symptoms			Percentage of Calories			
					Pulse	Thyroid Enlargement	Tremor	Type of Goiter	Protein	Fat	Carbo- hydrate
1	Armstrong.....	♀	30	49	120	Large	+++	Mixed	8.1	32.8	59.1
2	Baker.....	♀	41	57	88	Large	++	Toxic adenoma	6.8	35.0	58.2
3	E. B.	♀	35	22	85	Visible	+	Toxic adenoma	9.7	35.0	55.3
4	F. C. B.	♀	43	27	104	Visible	++	Exophthalmic	0.6	38.2	59.2
5	Blank.....	♀	50	14	94	Visible	+	Exophthalmic	11.1	32.1	56.8
6	Bryan.....	♀	37	50	95	Medium	++	Mixed	10.1	40.1	49.8
7	Capone.....	♀	54	66	124	Very large	++	Toxic adenoma	7.1	35.3	57.6
8	Eggleston.....	♀	45	18	92	Very large	+	Toxic adenoma	9.2	38.8	52.0
9	W. E.*.....	♀	53	28	86	Unilateral	+++	Exophthalmic	10.0	35.2	54.8
10	Fr. F.*.....	♀	34	14	88	Large	++	Toxic adenoma	10.4	33.6	56.0
11	Fobes.....	♀	45	22	96	Large	+	Toxic adenoma	9.1	36.2	54.7
12	M. Frank.....	♀	42	20	106	Large	++	Toxic adenoma	10.1	35.3	54.6
13	M. Fried.....	♀	24	63	124	Unilateral	+++	Exophthalmic	9.3	45.0	45.7
14	Goldstein.....	♀	50	65	84	Large	++	Toxic adenoma	10.6	33.7	55.7
15	Hofnar.....	♀	45	29	80	Visible	?	?	7.9	31.4	60.7
16	Holmberg.....	♀	46	28	104	Visible	++	Toxic adenoma	10.7	36.6	52.7
17	E. H.	♀	40	34	92	?	?	?	7.5	32.1	60.4
18	H. I.	♀	20	62	106	Large	+++	Exophthalmic	9.0	26.4	64.6
19	Jaroski.....	♀	29	12	88	Palpable	+	?	8.9	35.0	56.1
20	Klein.....	♀	25	55	140	Very large	+++	Exophthalmic	10.3	33.5	56.2
21	M. L.	♀	38	13	93	Visible	++	Toxic adenoma	9.3	24.6	66.1
22	F. L.	♀	30	14	102	Large	+	Toxic adenoma	8.3	39.7	52.0
23	Lawall.....	♀	24	31	90	?	?	?	10.1	36.2	53.7
24	K. L.	♀	30	16	80	Medium	+	?	9.2	34.1	56.7
25	W. A. L.*.....	♀	43	90	112	Large	+++	Exophthalmic	9.9	43.6	46.5
26	F. L.	♀	39	35	120	Medium	+++	Mixed	11.0	45.2	43.8
27	C. M. M.	♀	24	46	122	Large	++	Toxic adenoma	10.0	30.7	59.3
28	McC.....	♀	67	43	108	Large	+++	Mixed	10.3	43.4	47.3
29	S. N.	♀	50	53	92	Medium	+++	Mixed	9.3	33.2	57.5
30	G. N.	♀	24	35	96	Medium	++	Mixed	10.5	20.0	69.5
31	S. P.	♀	59	33	96	Medium	++	Exophthalmic	10.1	33.2	56.7
32	Paulhek.....	♀	52	39	110	Medium	++	Toxic adenoma	10.1	27.1	62.8
33	Risberg.....	♀	56	18	108	Egg size	+++	Toxic adenoma	10.3	35.2	54.5
34	Rooks.....	♀	47	34	88	?	?	?	6.3	30.7	61.0
35	Slaughter.....	♀	41	23	102	Large	+++	Toxic adenoma	8.0	29.2	62.8
36	F. T.	♀	33	36	104	Large	++	Exophthalmic	10.0	32.0	58.0
37	Todd*.....	♀	40	55	104	Medium	+++	Exophthalmic	8.3	36.4	55.3
38	Ward.....	♀	26	25	100	Visible	?	?	10.0	40.3	49.7
39	Whitney.....	♀	58	32	96	Large	+++	Toxic adenoma	9.2	38.7	52.1
40	Stricker*.....	♀	33	12	96	Medium	?	?	9.6	30.6	59.8

* Recurrent goiter.

roidectomy and after the usual drop to a subnormal basal metabolic rate, i. e. when all need for food concentrated in calories is past, a high percentage of patients will persist in this preference for a low protein diet for months or perhaps for the remainder of their lives.

Moreover, the total calory requirement of the toxic goiter patient is frequently even smaller than that of a normal subject of equal size, thus showing that high calory demand does not explain this peculiar imbalance of the protein portion of the diet.

CLINICAL APPLICATION

Thyroid enlargement as a sign of toxic goiter is too variable to be of much value in diagnosing hyperthyroidism of any degree, especially if the disease is just beginning. Many workers also admit the possibility of the presence of toxic goiter in beginning or subclinical form in individuals showing normal basal metabolic rates. Thus, if the basal metabolic rate before

From this study it appears that they may be classified under one heading, namely, subclinical goiter. Besides resembling the clinical stage of toxic goiter except in thyroid enlargement and increased basal metabolic rate, this condition shows an additional point of similarity to toxic goiter, namely, an identically similar habitual protein deficiency (below 12 per cent protein calories) in the self-selected diets of such patients.

These physically depressed, emotionally unstable patients in any medical practice greatly outnumber the clinically toxic ones, just as do those with subclinical rickets, subclinical pellagra or any nutritional disease in which the beginning manifestations evolve progressively to an entirely different final picture in its full-grown stage.

The number of such cases encountered in this study have outnumbered the forty cases of clinically toxic goiter listed in table 4 by about five to one. The record of this larger series and a description of the surprisingly good therapeutic results achieved through the use of a

normal protein diet in these cases (including cases of persistent and recurrent toxic goiter following thyroidectomy) cannot logically be included in this report. They will be presented in a future paper, together with the description of a greatly simplified laboratory routine for measuring protein deficiency in both clinical and subclinical toxic goiter without the use of the complicated procedures required for collection and analysis of all of the diet in the work here reported.

CONCLUSIONS

The results of 233 analyses of the self-selected diets of 154 normal, healthy subjects of various ages, races and occupations, and 117 analyses of the diets of forty toxic goiter patients have shown that each individual is guided by personal food preference to select a diet which he maintains at a relatively constant protein percentage and at a level characteristic of himself.

A protein content of 13 per cent is sufficient; one of 11 per cent is insufficient, and yet the individual who prefers the 11 per cent diet, when placed on a diet containing 13 per cent will unconsciously tend to revert to the 11 per cent level without the remotest idea as to how much protein either diet contains.

Once this subconsciously operating personal food preference becomes inaccurate in its selection of a proper protein percentage, it may be reeducated or redirected to its former degree of accuracy only with considerable coaching and perseverance. Indeed, the subconscious reactions which determine the level at which this constant protein percentage shall be established by the individual apparently lie deeper than mere temporary physiologic need, indicating that neither personal food preference, hunger nor appetite are to be trusted implicitly in the self selection of diets.

SUMMARY

Analysis by others of the total food consumed by large groups of active, normal persons has established the normal protein content at from 13 to 17 protein calories per hundred calories of food, i. e., from 13 to 17 per cent protein calories.

A routine was adopted for collecting and analyzing the self-selected diet in determining how far the individual has deviated from this normal in his dietary habits.

It is noteworthy that the lowest reported normal protein value is 13 per cent. A habitual personal preference for a diet containing appreciably less than this minimal limit of 13 per cent protein calories is of clinical importance because of its ultimate effect on health.

Persons suffering from toxic goiter—regardless of age, sex or type of goiter—uniformly show a tendency to select a diet below this minimal limit of 13 per cent protein calories.

When put on a diet containing the normal percentage (13 per cent) of protein the toxic goiter patient tends constantly to revert to his own preference for the sub-normal protein diet.

Preference for a low protein diet persists in variable degree even after subtotal thyroidectomy in a high percentage of cases and is uniformly associated with unfavorable postoperative results, such as fatigue and susceptibility to cold, and in some cases with actual recurrences of the disease.

315 South Honore Street.

CONTRACEPTION: A STUDY OF FIVE HUNDRED CASES FROM PRIVATE PRACTICE

CLINICAL OBSERVATIONS

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NEW YORK

An analysis of 500 private contraceptive cases selected at random from my files is presented. This study shows the extent and types of contraception practiced during a twelve year period, before and after medical consultation, by a group of middle class New York city families of different religious denominations, all of whom were white but three.

I interviewed each of the 500 women in this study and gave a general physical examination, including a bimanual pelvic examination.

TABLE 1.—Reasons Patients Requested Contraceptive Advice

1. Recent childbirth
2. Desire to space offspring
3. Desired number of children already born
4. Medical condition of wife, e. g., hyperthyroidism, nephritis, tuberculosis, diabetes, heart disease, deaf-mutism, blindness or convalescence after acute illness such as typhoid fever or pneumonia, or after surgical procedure such as appendectomy, or rectal fistula
- Medical condition of husband, e. g., heart disease, tuberculosis, convalescence from surgical procedure or acute illness
5. Mental illness or emotional disturbance of husband or wife
6. Economic conditions (a) Unemployment of husband
(b) Wife sole or co-wage earner
(c) Support of dependents
(d) Desire to complete education or professional training
(e) Indebtedness
7. Dissatisfaction of either or both partners with method of contraception employed
8. Failure of method employed

TABLE 2.—Marital Status at Time of Consultation for Contraceptive Advice

Marital Status	Number of Women	Per Cent
Married.....	363	73.6
Unmarried.....	132	26.4
(a) Engaged.....	93	19.2
(b) Unattached.....	39	7.2
Total.....	500	

The purpose of this clinical study was to ascertain the extent and efficiency of contraceptive efforts and their influence on fertility and marital happiness. The results of medically prescribed contraceptive methods are compared with self-prescribed methods. The health problems involved are summarized.

A variety of factors which might affect the health of the wife, the size of the family and marital happiness were studied. Information was obtained about the physical and emotional health of the husbands and wives, their social, economic and educational status and their religious beliefs. Intimate facts are given regarding their sex habits, contraceptive methods, failure and success of contraceptive methods, size of families, number of planned and unplanned pregnancies, number of abortions, premarital sex experiences, frequency of coitus, frequency of orgasm, sexual compatibility, pelvic pathologic conditions and other factors, and conclusions are summarized in the accompanying tables.

The majority of women in this study (368) consulted a physician for contraceptive advice after marriage. The largest number (125) applied during the first year of marriage, the second largest group (ninety-four) came between the second and the fifth year and a close tie were ninety-three women who came premaritally. By

TABLE 3.—Duration of Marriage at Time of Consultation

Number of Years Married	Number of Women	Cumulative Totals of Number of Women
1 day to 1 month.....	46	...
1 to 6 months.....	51	...
7 to 12 months.....	28	...
During 1st year.....	125	...
Total married 1 year.....	...	257
1 to 5 years.....	94	...
Total married 5 years.....	...	351
6 to 10 years.....	68	...
Total married 10 years.....	...	419
11 to 15 years.....	42	...
Total married 15 years.....	...	461
16 to 20 years.....	21	...
Total married 20 years.....	...	482
21 to 30 years.....	5	...
Total married 30 years.....	...	487
Unknown.....	13	...
Total.....	...	500

TABLE 4.—Religious Distribution

Denomination	Number of Men	Number of Women
Hebrews.....	239	245
Protestants.....	136	175
Catholics.....	59	58
Unstated.....	26	22
Mixed marriages: Hebrew and Catholic.....	5	
Hebrew and Protestant....	1	

the end of the fifth year 351 had applied and after ten years 461 had asked for medical aid in controlling reproduction. In recent years there has been an increased trend toward seeking contraceptive advice premaritally. The ideal time to give medical contraceptive advice is premaritally if conception must be avoided for health reasons. Sixty-eight women applied ten years and twenty-six came between sixteen and thirty years after marriage. Thirty-nine single (unattached) women requested contraceptive advice.

The majority of women (91 per cent) were married before 35 years of age; of these 44 per cent married before 25, 16 per cent married between 35 and 50, 8 per cent married between 36 and 40 and 7 per cent between 40 and 50. Two-tenths per cent married after 50.

Eleven wives were from one to six years older than their husbands, all others the same age or younger. In one case only was there a great difference — that of a man of 50 with a wife of 25 years.

The husbands ages ranged from 17 to 60 years. The majority of men, 207, or 40.5 per cent, married before 29 and 176, or 38.1 per cent, between 30 and 40 years; while a minority, sixty-six, or 14.3 per cent, married between 40 and 60. Most men who intended to marry did so before 40 years. The majority of women in this study married earlier, before 25, while the majority of men married between 25 and 35. By the age of 35 the majority of men and women were married.

Over half the women in this series were gainfully employed of necessity and were co-wage earners. (These figures may be higher because of the larger number of young wives.) Ninety per cent of the premarital group stated that they would have to continue working after

marriage and 10 per cent wished to do so. Economic insecurity was the biggest single factor given for seeking contraceptive advice and avoiding immediate pregnancy. Every premarital couple expressed the request that the method prescribed should not cause sterility and stated that they hoped to be able to plan a pregnancy as soon as their financial status would allow them to rear a child according to desirable standards of living.

Of the 229 who admitted adequate income, many stated that they already had all the children they could afford or that they wished to space further pregnancies scientifically for health or social reasons.

Thirty-eight per cent of ninety-three engaged couples who came for a premarital medical consultation admitted premarital sex relations, mostly during the engagement period, whereas 62 per cent denied premarital sex experience. Of those married at the time of consultation only 9.2 per cent admitted premarital sex relations whereas 91 per cent denied them. Seventy-seven women, or 15 per cent of the 500 women, were virgins. Of these there were 6.5 per cent married virgins and 57 per cent of the engaged with intact hymens.

(Since the study of 500 cases, another study of 170 premarital couples seen from January 1938 to December 1939 was made. Premarital sex relations were admitted by 36 per cent of the females and 51 per cent of the males. Of this group 100 were college graduates, sixty high school graduates and 9 elementary school graduates between 18 and 35 years of age. Forty-one virgins of this group required medical dilation of the hymen due to various anatomic reasons, such as small hymenal opening, and eighty-eight after medical inspection were told they required no medical stretching of the hymen and introitus.)

TABLE 5.—Age of 461 Couples at Marriage

Age	Number of Men	Percentage of Men	Number of Women	Percentage of Women
15-19.....	1	0.2	1	0.2
20-23.....	52	17.7	203	44.4
24-30.....	123	27.1	108	23.4
31-35.....	120	26.0	107	23.2
36-40.....	56	12.1	39	8.4
41-50.....	61	13.2	34	7.3
51-60.....	5	1.08	1	0.2

TABLE 6.—Employment of Wives in Relation to Duration of Marriage

Total number of women employed.....	276
Married women employed.....	144
Premarital group of women planning to continue employment after marriage.....	122

TABLE 7.—Relation of Combined Incomes to Number of Children Desired (Planned Future Pregnancies)

Total number of women.....	30
Combined incomes held inadequate.....	24
Combined incomes held adequate.....	229
Unknown ...	27

Either a much larger percentage of engaged couples are having premarital sex relations today as compared with the past, or the older married women are less frank in discussing this phase of their sex life.

Twenty-four married women required dilation of the hymen or removal of a septate band by electric cauterization at periods after marriage varying from one day to sixteen years. This was accomplished as an office

procedure usually in one medical visit. All needed psychotherapy to overcome fear of pain with coitus and instruction regarding male and female genital anatomy and sex technic. Only one patient required hospitalization and surgical dilation under nitrous oxide-oxygen anesthesia.

TABLE 8.—Premarital Sex Relations and Virginity

Status	Number Admitting Relations	Per Cent	Number Denying Relations	Per Cent	Intact Hymens	Per Cent
93 engaged women....	40	38.0	59	62.0	53	57.0
368 married women....	33	9.2	335	91.0	24	6.5

TABLE 9.—Nonconsummation of Marital Relations in Married Women

(Duration of Marriages and Causes)		Duration of Marriage at Time of Consultation
Number of Married Virgins		
4.....		1 week
2.....		2 weeks
2.....		3 weeks
2.....		1 month
3.....		2 months
1.....		3 months
2.....		6 months
1.....		11 months
3.....		1 year
1.....		3 years
1.....		7 years
1.....		10 years
1.....		16 years
Total 24		
Causes of Nonconsummation		
1. Septate hymen		
2. Tight thick hymen		
3. Fear of pain or inability to stand pain		
4. Ignorance of sex technic, either partner		
5. Ignorance of genital anatomy		
6. Fear of pregnancy		
7. Sense of shame regarding genitals and coitus		

The frequency of coitus in married couples before medical consultation was most often (39 per cent) twice a week, next (23 per cent) three times weekly and (19 per cent) once a week. Six per cent had daily sex relations while 2.3 per cent abstained. The majority of couples, 130, or 78 per cent, had intercourse more than once a week.

The use of prescribed contraceptive methods did not vary the frequency of coitus when sex habits had been established. The only significant change was the fact that only 0.5 per cent continued abstinent after the consultation whereas 2.3 per cent had had no sex relations before.

Twenty-six (10.3 per cent) single women had been pregnant once out of wedlock, nine women during their engagement period and fourteen unattached women. Two unmarried women had been pregnant twice. One single woman had been pregnant four times.

Of 500 women of childbearing age in this study, 368 were married at the time of consultation and 132 were unmarried. Ninety-three engaged women came for premarital consultations. Two hundred and fifty-two (50.4 per cent) had been pregnant from one to twelve times and had had 581 pregnancies. Three hundred and fifty-four (60 per cent) were accidental pregnancies and 227 (40 per cent) were planned.

One hundred and eighty-one (71.8 per cent) women had been accidentally pregnant with 354 unplanned pregnancies and 134 (53 per cent) had had 227 planned

pregnancies. By comparison there were one-fifth (19 per cent) more women who had accidental pregnancies. Of the 252 women who had been pregnant, 112 (48 per cent) had been pregnant once, sixty-three (25 per cent) twice, thirty-four (13 per cent) three times, twenty-five (9.9 per cent) four times, eight (3 per cent) five times, four (1.5 per cent) six times, five (1.9 per cent) seven times, one (0.4 per cent) eight times, one (0.4 per cent) ten times, and two (0.8 per cent) twelve times.

Of the 368 women married at the time of consultation, 221 (50 per cent) had been pregnant one to twelve times. Of these, 131 (59.3 per cent) of the group of married women had planned pregnancies and 153 (69.2 per cent) had accidental (unwanted) pregnancies. Of the total 134 women who planned 227 pregnancies, sixty-two (46 per cent) planned one pregnancy, fifty-three (39 per cent) planned two pregnancies, fifteen (11 per cent) planned three, two (1.4 per cent) planned four and one (0.7 per cent) planned six. Two hundred and forty-eight (49.6 per cent) of the 500 women had never been pregnant. Of these nulliparous women, 147 (40 per cent) were married at the time of consultation and 101 (76.5 per cent) came premaritally.

Of the 181 women accidentally pregnant, 106 (54 per cent) had one unwanted pregnancy; thirty (16 per cent) had two accidental pregnancies, fourteen (7.8 per cent) had three, thirteen (7.2 per cent) had

TABLE 10.—Frequency of Coitus in Marriage

Frequency of Coitus	(Figures Obtained for 177 Cases)		Before Consultation		After Consultation	
	Number of Women	Percentage of Women	Number of Women	Percentage of Women	Number of Women	Percentage of Women
None.....	4	2.3	1	0.5		
	4	2.3	6	3.5		
	6	3.5	2	1.1		
Once a week.....	33	19.0	35	20.0		
Twice a week.....	66	39.0	53	31.0		
Three times a week.....	40	23.0	41	24.0		
Four times a week.....	8	4.6	15	8.9		
Five times a week.....	6	3.5	11	6.5		
Daily.....	10	6.0	8	4.9		

TABLE 11.—Fertility of 500 Women

(Parity in Married and Premarital* Groups)									
Marital Status	Total Number	Nulliparous Women		Multiparous Women—Parity 1-12 Times		Women with Planned Pregnancies		Women with Accidental (Unwanted) Pregnancies	
		Num-ber	Per Cent	Num-ber	Per Cent	Num-ber	Per Cent	Num-ber	Per Cent
Married and unmarried women	500	249	49.6	252	50.4	134	53.0	181	71.8
Married women	368	147	40.0	221	60.0	131	59.3	153	69.2
Premarital women	132	101	76.5	31	23.5	3	9.7	25	90.3
93 engaged									
39 single									

* The "premarital group were those seen prior to marriage but who after marriage had pregnancies as classified. A small group, twenty-six, 10 per cent of the 252 parous women or 5 per cent of the total group of 500, had been pregnant out of wedlock or truly premaritally.

four, four (2.2 per cent) had five, six (3.3 per cent) had six; two (1.1 per cent) had eight and one each (0.5 per cent) had eleven and twelve.

Three single women were diagnosed as pregnant at first consultation; one two months, one three and one-half months and one five months pregnant. The largest cause for accidental pregnancies in the premaritally

instructed and single group was condoms breaking, nine cases; next, withdrawal, seven cases; five women used no precautions, three inserted vaginal diaphragms incorrectly, failing to cover the cervix, and two became pregnant using just a douche. In two cases the causes were

TABLE 12.—*Gravidity Analysis of Women with Planned and Unplanned Pregnancies*

Gravida, Number of Times Pregnant	Women Pregnant 1-12 Times			Women Accidentally Pregnant			Women with Planned Pregnancies		
	Married	Premarital Group	Totals of 500 Women	Married	Premarital Group	Totals of 252 Women with Pregnancy	Married	Premarital Group	Totals
0	147	101	248
1	88	24	112	81	25	106	60	3	63
2	60	3	63	28	2	30	53	..	53
3	33	1	34	13	1	14	15	..	15
4	24	1	25	11	2	13	2	..	2
5	8	..	8	4	..	4
6	4	..	4	6	..	6	1	..	1
7	5	..	5
8	1	..	1	2	..	2
9
10	1	..	1
11	1	..	1
12	2	..	2	1	..	1

TABLE 13.—*Number of Pregnancies, Planned and Unplanned*

	Number of Pregnancies	Number of Accidental Pregnancies	Percentage of Accidental Pregnancies	Number of Planned Pregnancies	Percentage of Planned Pregnancies
Married group....	540	315	58.0	225	42.0
Premarital group	41	39	95.1	2	4.9
Totals.....	581	354	60.2	227	39.8

not known. The contraceptive pessary was not used by any of the unattached women. All of this group were having sexual relations before consultation.

The average size of the family was 1.8 children per mother. Forty-three per cent had one living child, 40 per cent had two children, 11 per cent had three, 2.3 per cent had four, 1.7 per cent had five and 0.5 per cent had eleven. One pair of twins occurred in 314 living births.

In this study the usual family consisted of one or two children; occasionally there were three and exceptionally four or five. There were rarely more than five children.

Planned pregnancies occurred mostly between 21 and 29 years of age, the majority, seventy-six before 25 years. There were ninety-five planned pregnancies before 30, and twenty-two between 30 and 40 years. There was little difference between the ages of the majority of planned and accidental pregnancies, except that more accidental pregnancies occurred between 35 and 45 years of age. There were decidedly fewer unplanned pregnancies in the premaritally instructed group.

Of 252 pregnant women, 106, or 42 per cent, admitted to 151 abortions. Sixty-eight, or 64 per cent, had had one abortion and twenty-two, or 20 per cent, had had two abortions. One admitted to eight abortions.

Comparison of twenty-five criminal abortions after scientific contraception with 127 before indicates the ability of medically prescribed birth control to decrease the number of criminal abortions to one fifth, with subsequent prevention of maternal morbidity and possible sterility. The majority of abortions occurred in married women.

The sexual adjustment of the husband was given as improved in 342 cases after consultation and the same or unimproved in fifty-one cases.

Of ninety engaged couples who came for premarital sex advice, fifty-nine, or 65.5 per cent, of the men had not had sexual experience and thirty-one, or 34.5 per cent had had sex relations. Practically two thirds of the engaged men in this study had remained abstinent until marriage. Forty-one of the 368 women in the married group expressed dissatisfaction with their husband's sexual ability. Three complained of impotence, fifteen of premature ejaculation and twenty-three of inadequate sex relations. The rest complained of the husband's lack of interest in preliminary love play, manual stimulation or selfishness. A few complained of distaste for husbands due to halitosis, unhygienic body care, fear of venereal disease and odious comparisons with other sex partners.

When medical contraceptive advice is not obtained, the man is relied on for assuming contraceptive measures. Three hundred and fifty-six husbands (81 per cent) practiced contraception: by use of condoms alone in 235 cases (52 per cent) and alone or in combination with jelly, suppository or douche in 265 cases (60 per cent), while coitus interruptus was used in ninety-one cases (20 per cent), alone in eighty-six cases and combined with a douche in five cases.

TABLE 14.—*Reasons for Accidental Pregnancies in Single Women and Those Premaritally Instructed*

	Number of Women Accidentally Pregnant		Cause and Number of Times Contraceptive Method Failed					
	Pregnant Once	Pregnant Twice	Pregnant 4 Times	Unknown	Condom Broke	Withdrawal	Douche	Poor Technique Vaginal Diaphragm Nothing Used
Women with accidental pregnancies after receiving contraceptive advice premaritally (9)	9	2	2	1	..	3
Single (pregnant out of wedlock before consultation (17))	14	2	1	..	7	6	2	4
Total number of women (26)	23	2	1	2	9	7	2	7

TABLE 15.—*Size of Family*

Total number of women with living children.....	171
Total number of living children.....	314
Number of stillbirths.....	7
Average number of children per mother.....	1.8

Multiple births—1 pair of twins among 314 living children born to 171 pregnant mothers.

TABLE 16.—*Distribution of Size of Family*

Number of living children per mother	1	2	3	4	5	11
Number of women.....	74	69	20	4	3	1
Percentage of women.....	43.0	40.3	11.0	2.3	1.7	0.5

The woman relied on the douche alone and in combination in 90 cases (20 per cent). "Feminine hygiene," or use of contraceptive jellies alone and in combination, was practiced by forty-six (10.5 per cent). Vaginal diaphragms were used by thirty (6.8 per cent), cervical caps by five (1 per cent). Occlusive pessaries were used by only 8 per cent of the women before medical consultation. Fourteen, or 3.2 per cent,

resorted to vaginal suppositories alone or in combination. Only three (6.8 per cent) used the "safe period" and one (0.2 per cent) used lactation. Four (0.8 per cent) practiced abstinence and two (0.4 per cent) had external coitus. Twenty-five (5.7 per cent) used no contra-

TABLE 17.—Age of Pregnant Women

A. Unplanned Pregnancies			B. Planned Pregnancies		
Age	Married Women	Premarital Women	Age	Married Women	Premarital Women
16.....	2	1	19.....	7	..
17.....	3	3	20.....	10	..
18.....	6	1	21-23.....	59	1
19.....	7	1	26-30.....	29	1
20.....	10	4	31-33.....	21	..
21-25.....	53	5	36-40.....	1	..
26-30.....	33	7			
31-35.....	29	2			
36-40.....	5	2			
41-45.....	3	..			

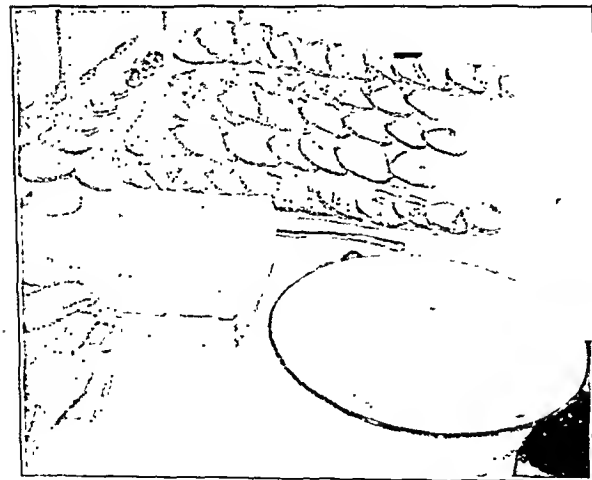
TABLE 18.—Pregnancy Wastage (Abortions, All Types)

	Totals							
Number of women.....	63	22	6	8	1	1	1	106
Number of abortions	1	2	3	4	7	8	8	151
Number of unmarried women (engaged or single).....	10	..	1	1				

TABLE 19.—Pregnancy Wastage (Criminal and Therapeutic Abortions)

	Number of Criminal Abortions	Number of Therapeutic Abortions
Before consultation for contraceptive advice	127	6
After consultation for contraceptive advice	25	7

ceptive, admitting that they did not want pregnancies but did not understand the process of conception and knew nothing of the possibility for contraception.



Types of medically prescribed contraceptive pessaries.

The choice and most frequent medically prescribed contraceptive method was the use of a vaginal type occlusive rubber diaphragm lubricated with a spermicidal jelly or cream. Of the 500 women examined, fifty-three had no method prescribed because of such reasons as sterility, existing pregnancy or operation required for pelvic abnormality. Of the 447 women given birth con-

trol advice, 413 (92.3 per cent) were fitted and instructed in the use of rubber occlusive pessaries, 406 (90.8 per cent) vaginal type diaphragms and seven (1.5 per cent) cervical caps. Twenty-six (5.8 per cent) women preferred to have the husband use condoms and seven of these also injected jelly intravaginally before coitus. The modern method places the contraceptive measure in the hands of the wife. The sizes of vaginal diaphragms most frequently used were No. 80 (140 cases), No. 75 (116 cases), No. 85 (sixty-two cases), No. 70 (fifty-four cases), No. 90 (twenty-one cases),

TABLE 20.—Sexual Experience and Adjustment of Husbands

	Premarital Sex Experience	No Premarital Sex Experience	Impaired Sex Ability	Premature Ejaculation	Impotence
Husbands of married group.....	34	?	23	15	3
Male partners in engaged group...	31	59

TABLE 21.—Contraceptive Methods Used by 437 Couples Before Consultation

A. Contraceptive Methods	Frequency of Use	
	Number of Cases	Per Cent
Condom	230	...
Coitus interruptus	56	...
Douche	23	...
Suppository	7	...
Safe period (rhythm theory).....	3	...
Nothing	25	...
Gold stem wishbone type pessary.....	1	...
Vaginal diaphragm (rubber).....	30	...
French pessary (cervical type).....	2	...
Luteal pessary	3	...
Contraceptive jelly alone.....	4	...
Coitus interruptus and douche.....	5	...
Condom and suppository	3	...
Condom and douche	23	...
Condom and jelly	7	...
External coitus	2	...
Lactation	1	...
Suppository and douche.....	4	...
Abstinence	4	...
B. Male Methods of Contraception		
Condoms alone and with jelly, suppository or douche	265	60.6
Coitus interruptus alone and with douche.....	91	20.7
Total male methods.....	356	81.3
C. Female Methods of Contraception		
Douche alone	23	...
Douche and condom	25	...
Douche and coitus interruptus	5	...
Douche and suppository	4	...
Douche and diaphragm	30	...
Total douche alone and in combination.....	92	20.0
Vaginal diaphragm	30	6.8
Cervical type pessaries.....	5	...
Stem pessaries (intracervical).....	1	...
Jelly alone	4	...
Jelly with diaphragm	23	...
Jelly with cervical type pessaries.....	5	...
Jelly with condoms.....	7	...
Total jelly alone and in combination.....	46	10.5
Suppositories alone	7	...
Suppositories and condom	3	...
Suppositories and douche	4	...
Total suppositories alone and in combination	14	3.2
Safe period	3	0.63
Lactation	1	0.2
D. Other methods		
External coitus	2	0.4
Abstinence	4	0.8
Nothing used (pregnancy not desired).....	25	5.7

No. 65 (seven cases), No. 60 (three cases), No. 95 (two cases) and No. 100 (one case).

The average size of vaginal diaphragm used was No. 80 with No. 75 ranking second and No. 85 in third place. No. 65 or smaller is seldom required, while No. 90 is fairly frequent.

(The vaginal diaphragm extends from behind the symphysis pubis along the anterior vaginal wall to the posterior fornix behind the cervix, not serving just as a cervical cap.)

Where anatomic reasons preclude fitting with vaginal diaphragms, a cervical type is prescribed. This is a suction cap covering just the cervix, also lubricated with contraceptive jelly or cream. (Cervical types are more difficult to place and easier to dislodge. Careful technic is required.)

When no type of occlusive pessary can be fitted, or when the woman refuses to use one, the only other reliable method is the use of the condom. With proper technic and instruction this method is highly reliable but has many disadvantages which the diaphragm method overcomes.

Disadvantages of the condom method are:

1. Many husbands cannot or will not use condoms.
2. Lack of knowledge of testing and proper use are responsible for frequent failure due to breaking, leaking or the condom slipping off.
3. Chemical preservatives or nonlubrication causes irritation to male and female genitals.
4. Physiologically it is difficult for some women to reach orgasm before the husband ejaculates; the condom prevents a normal female climax.
5. It is psychologically undesirable to some men and women, as it interrupts love play.
6. It diminishes sensation for both partners.
7. It is more expensive than the pessary method.

One woman had four failures. Another wife conceived extramaritally thinking she was sterile; her husband was found to be sterile.

There were 180 cases of failure reported due to: (1) condoms, seventy-two cases (40 per cent); (2) with-

saries, two cases (1.1 per cent); (9) gold stem wish-bone pessary, one case; (10) believed herself sterile, one case (0.5 per cent).

Use of vaginal diaphragms was 97.6 per cent successful as a contraceptive method. It was the most efficient method that was used. The causes for failure were due

TABLE 24.—Number of Women Using Contraceptive Methods Successfully and Time of Use

(All Types—No Unplanned Pregnancies)	
Time	Number of Women
From 1 to 6 months.....	13
6 to 12 months.....	21
12 to 17 months.....	71
18 to 24 months.....	71
2 to 3 years.....	57
3 to 4 years.....	47
5 to 9 years.....	79
10 to 14 years.....	45
15 to 19 years.....	27
20 to 24 years.....	12
25 to 30 years.....	5

TABLE 25.—Causes of Failure of Contraceptive Methods

(All Types—180 Cases Reported)	
Method Used Which Failed	Number of Women with Unwanted Pregnancies
Condoms.....	72
Withdrawal.....	43
Douche.....	24
Nothing used.....	16
Vaginal diaphragm.....	10
Vaginal suppositories.....	8
Vaginal jelly alone.....	3
Cervical pessaries.....	2
Gold stem pessaries.....	1

TABLE 26.—Analysis of Ten Vaginal Diaphragm Failures

(413 diaphragms used, 36 fitted elsewhere—2.4 per cent failures)	
Reasons for failures	
1. Poor technic in application; inserted into anterior fornix (cervix uncovered)	
2. Failure to feel the cervix covered	
3. Immediate removal after use without a douche	
4. Improper fitting; wrong size or type	
5. Acknowledged omission of diaphragm on occasion; "took a chance"	
6. Discontinued use; lazy, too much trouble	
7. Inserted only at end of coitus	
8. Lanteen type used without fitting or instruction or fitting	
9. Used same size without refitting after delivery (required larger size)	
10. Purchased diaphragm in drug store and used without instruction	

to human elements, either improper fitting and improper type prescribed or improper use, careless technic or lack of use. There was no case of unexplained failure. No sterility was caused by use of an occlusive diaphragm or cervical cap.

Acute gonorrhea was diagnosed in seventeen women and two cases of syphilis were disclosed and treatment was advised for women who came for contraceptive advice. Not one of these women was aware of the nature of her disease.

SUMMARY

A study of 500 private contraceptive cases is presented, in 94.3 per cent of which contraception was admittedly being practiced before the medical consultation. The cases are drawn from various religious, age and economic groups. The women requested contraceptive advice for a variety of health, psychologic and economic reasons. More than 50 per cent (276) of the women in this study were employed of necessity. Ninety per cent of the "premarital" group stated that they had

TABLE 22.—Medically Prescribed Contraceptive Methods

Contraceptive Methods	Number of Cases
Vaginal diaphragms (rubber, coiled and watch spring rins) with spermicidal jelly or cream.....	406
Cervical type occlusive pessary.....	7
(a) Dumas	3
(b) Mizpah	4
Total occlusive pessaries.....	413
Condoms alone	19
Condoms with jelly.....	7
Total use of condoms.....	26
No method prescribed	53

TABLE 23.—Sizes of Vaginal Diaphragms Prescribed

Sizes (Mm.)	Number Prescribed
60.0.....	3
65.0.....	7
70.0.....	54
72.5.....	22
75.0.....	94
77.5.....	27
80.0.....	113
82.5.....	12
85.0.....	50
87.5.....	2
90.0.....	19
95.0.....	2
100.0.....	1

drawal, forty-three cases (23.8 per cent); (3) douche alone, twenty-four cases (13.3 per cent); (4) nothing used, sixteen cases (8.8 per cent); (5) vaginal diaphragm, ten cases (5.5 per cent); (6) vaginal suppositories, eight cases (4.4 per cent); (7) contraceptive pills, three cases (1.6 per cent); (8) cervical pess-

to continue working after marriage. Half of the group of 500 stated that inadequate income was their main reason for wanting to avoid further pregnancies.

The majority of women sought contraceptive advice during the first year of marriage, the remainder from one to thirty years after marriage. The trend among the younger group is toward obtaining contraceptive advice premaritally.

Fifty-seven per cent of the unmarried and 6.5 per cent of the married women had intact hymens. Most of these required medical dilation. Thirty-eight per cent of those seeking premarital advice were already having sex relations.

Fifty-three per cent of the women had planned pregnancies, usually one or two children, the average being 1.8 children per mother. Of all the pregnancies, 60 per cent were accidental and resulted from the failure of various types of contraception. An analysis of these failures is given. Five per cent of the total group had been pregnant before marriage. Very few accidental pregnancies occurred in the group instructed premaritally.

TABLE 27.—Reasons Potents Discontinued Use of Any Contraceptive

(96 cases reported)	Number of Cases
1. Planned pregnancies	24
2. Pregnancy diagnosed first visit (accidentally pregnant) ..	35
3. Female sterility (diagnosed by Rubin test, operation, laboratory reports)	17
(a) Closed tubes	4
(b) Fibroids or hysterectomy	9
(c) Oophorectomy	2
(d) Menopause	1
4. Wife erroneously believed herself sterile	2
5. Male sterility	4
(a) Undescended testicles	1
(b) Impotence	2
(c) Husband insane	1
6. Divorced, separated, widowed, terminated sex relations ..	10
7. Laziness	2

TABLE 28.—Menstruation—Types and Character

Type	Number of Cases
Regular (28-32 day cycle)	407
Irregular	59
Dysmenorrhea (severe)	95

TABLE 29.—Pelvic Abnormality Found on Routine Pelvic Examination for Fitting Diaphragms

Pathologic State	Number of Cases
Pregnant on examination	38
History of oophorectomy and salpingectomy	7
.....	105
.....	142
.....	54
.....	64
.....	43
.....	39
.....	27
.....	7
.....	2
.....	17
.....	15
.....	2

A most important observation was that medically prescribed contraceptive advice reduced the number of abortions by four fifths. Forty-two per cent of the 252 parous women had had abortions. Sixty-four per cent admitted to one abortion and 36 per cent had had two or more abortions. The majority of abortions occurred in married women.

Before medical consultation 81 per cent of the husbands practiced contraception by the use of condoms or coitus interruptus and 20 per cent of the women used a douche.

The most frequent method which I prescribed was the vaginal diaphragm lubricated with a contraceptive jelly

TABLE 30.—Venereal Disease Statistics

	Gonorrhea	Syphilis
Number of husbands	0	1
Number of wives	17	2

TABLE 31.—Summary of Causes for Sexual and Marital Dissatisfaction

Reasons	Number of Wives
1. Fear of consequences of repeated abortions	129
2. Fear of unwanted pregnancy	229
3. Faulty contraceptive methods (inadequate opportunity for orgasm)	54
4. Dyspareunia (vaginismus, improper sex technic)	42
5. Fear of coitus	229
6. Ignorance of reproductive process and genital anatomy	24
7. Emotional frustration due to sterility	16
8. Aversion to coitus (frigidity)	37
9. No sex desire (low basal metabolism rate found)	9
10. Anatomic causes for unsatisfactory coitus	16
(a) Tight resistant septate hymen	
(b) Size and location of clitoris	
(c) Extreme obesity of either husband or wife	
(d) Infantile genital development	
(e) Pelvic abnormality, e. g. parametritis, torn perineum, retroversion	
(f) Irritating vaginal discharges	
(g) Dyspareunia	
11. Disparity in age	4
12. Venereal disease	6
13. Infidelity	5
14. Secret use of contraceptive by wife	2
15. Masturbation preferred to coitus	4
Other frequent complaints:	
16. Male sex inadequacy	
17. Prolonged debilitating illness of one partner	
18. Anxiety over economic insecurity (husband unemployed, wife sole wage earner)	
19. Manual clitoral stimulation preferred to coitus	
20. Too frequent pregnancies	
21. Cultural aesthetic inequalities	
22. Lack of privacy (poor housing)	
23. Husband's preference for perversions	
24. Faulty attitude of husband or wife toward normal sex and marriage intimacies	

or cream (90.8 per cent of the cases). The sizes most frequently prescribed were, in order, 80 mm., 75 mm. and 85 mm. This method proved to be 97.6 per cent effective and improved marital adjustment. The most frequent causes for sexual dissatisfaction are analyzed.

Every "premarital" couple expressed the desire for offspring in the future. They felt the need for temporary contraceptive advice and wanted the assurance that the method would not cause sterility.

Contraception is a health problem of importance both to the patient and to the physician and involves the welfare not only of the individual but also of society.

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Schizophrenic Thinking.—The peculiar qualities of schizophrenic thinking and behavior generally are dependent principally on four conditions: (1) the schizophrenic turns away from reality (introversion); (2) his thinking is dominated by his complexes (topics with a strong affective coloring) to an extent not seen in the normal; (3) he regresses to a childish or infantile or archaic mode of thought, and (4) his personality undergoes a progressive disintegration. These are not separate and distinct conditions but different aspects of one and the same thing.—Henderson, D. K., and Gillespie, R. D.: A Text-Book of Psychiatry for Students and Practitioners, London, Oxford University Press, 1940.

BLOOD SUGAR STUDIES ON GOLFERS

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Most sugar tolerance tests are performed on patients fasting and at rest, although many interesting studies have been made on persons during and after exercise.

The effects of exercise on blood sugar were first reported by Chaveau and Kaufmann.¹ They demonstrated as far back as 1886 that the blood sugar in a vein leading from the masseter muscle of a horse decreased on chewing. Weiland¹ in 1908 showed that venous blood sugar concentration was lower after exhausting exercise. In 1924 Levine, Gordon and Derick² showed that blood sugar levels decreased appreciably following exercise. Their studies were based on a group of runners who participated in the American marathon race of 25 miles in Boston, April 19, 1924. Working on the same general group of runners one year later, Gordon, Kohn and Levine³ demonstrated that the lowest blood sugar levels were found between the fourteenth and eighteenth miles. Those runners who were sustained during the race on a high sugar intake were much less fatigued than those who were not and performed better generally. Wollmer⁴ reported an immediate rise in blood sugar after exercise, followed

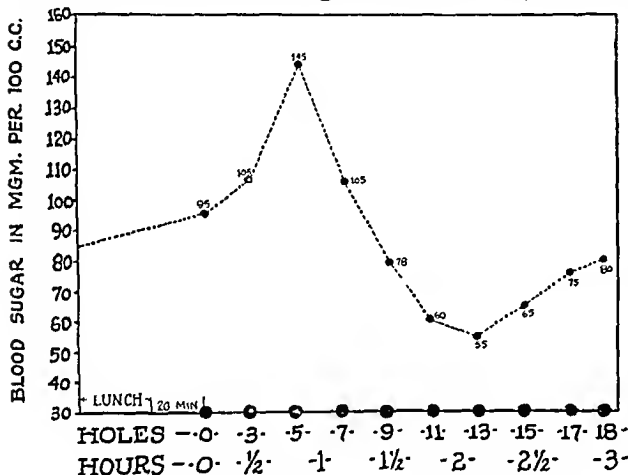


Chart 1.—Composite curve of blood sugar readings in a golf foursome taking three hours to complete. A definite drop begins at the ninth hole, reaching its lowest level at the thirteenth.

by a decline. He compared normal and obese subjects and found no appreciable difference in the two. Best and Partridge⁵ in their studies on Olympic athletes in 1928 described a depression in blood sugar levels following intense exercise. Strandell⁶ in 1934 and Boje⁷ in 1937 showed comparable manifestations among persons subject to measured amounts of exercise. The Smiths⁸ in 1937 demonstrated similar falls in normal individuals, but more pronounced drops in blood sugar

in diabetic patients following exercise. It was felt, therefore that studies should be undertaken on a sport played by a comparatively large number of people, namely golf, with the hope of evaluating some data which may be of practical use. There are at the present time over two million golfers⁹ playing on three thousand courses in the United States. Assuming that the greatest number of American golfers have handicaps ranging from 10 to 27, thirty subjects for the following experiment were taken from that group. They ranged from 35 to 45 years in age and were apparently healthy males with no evidence of diabetes. As far as possible these studies were performed under their normal playing conditions. They were allowed to eat their usual luncheons and played afternoon rounds of golf under normal conditions with the exception that they were not permitted to smoke during the tests. Blood sugar estimations were taken before and after lunch. (The tests were done by the Folin-Wu method on venous blood.) Thereafter blood specimens were taken at every odd numbered hole for the entire round. A composite average curve may be seen in chart 1. The postprandial rise reached its maximum at the fifth hole. At the seventh hole the blood sugar was down to 105 mg. per hundred cubic centimeters. From the eleventh to the fifteenth it was well below fasting. At the seventeenth hole it was almost back to the fasting, at which point it was carried on to the end, with a slight rise at the eighteenth hole. Chart 1 is the curve of an average foursome taking approximately three hours to complete. This curve is somewhat changed in a twosome, as the time element naturally influences the reaction (chart 2).

COMMENT

The lowest blood sugar readings were observed between the ninth and fifteenth holes in the case of a foursome and between the eleventh and the fifteenth in the case of a twosome. This period coincides with the time when the subjects complained mostly of fatigue. It was also during this period that the greatest number of poor shots were made by the golfers and the scores were the highest. The poorer golfers showed lower blood sugar curves in many instances because of the fact that they expended more energy in playing the game and showed greater signs of exhaustion. They also showed more evidence of mental and emotional fatigue as a result of their anxiety. This was probably part of a vicious circle, one factor influencing the other. The more high strung and excitable the subject, the more intense the mental fatigue. The more composed and accomplished golfers had fewer mental or physical changes during this period of hypoglycemia and their blood sugar did not descend to such low levels. In explaining this phenomenon two factors must be considered. The first is fatigue and the second anxiety,¹⁰ and the two are closely interrelated.

Muscular exercise results in the conversion of glycogen into lactic acid, one fifth of which is converted into carbon dioxide and water (glycolysis), but most of the remaining is reconverted into glycogen. In the liver, lactic acid is changed into glycogen, in which form it may be stored or liberated as dextrose into the blood stream. Glycogenesis in the liver is affected directly by the action of the pancreas (insulin). An increase in the utilization of dextrose by exercise is followed by an increase in hepatic glycogenolysis. In anxiety states there is probably an increase in the production of

1. Quoted by Strandell, B.
2. Levine, S. A.; Gordon, Burgess, and Derick, C. L.: Changes in Chemical Constituents of Blood Following a Marathon Race, *J. A. M. A.* 82: 1778 (May 31) 1924.
3. Gordon, Burgess; Kohn, L. A.; Levine, S. A.; Matton, Marcel; Scriver, W. de M., and Whiting, W. B.: Sugar Content of Blood in Runners Following a Marathon Race, with Especial Reference to the Prevention of Hypoglycemia: Further Observations, *J. A. M. A.* 85: 508 (Aug. 18) 1925.
4. Wollmer, M.: Blutzuckerspiegel und Muskelarbeit bei Gesunden und Fettsüchtigen, *Deutsches Arch. f. klin. Med.* 170: 122, 1931.
5. Best, C. H., and Partridge, R. C.: Observations on Olympic Athletes, *Proc. Roy. Soc. s. B.* 105: 323 (Sept. 2) 1929.
6. Strandell, B.: On the Influence of Exercise on the Blood Sugar, Especially in Connection with Dextrose Ingestion, *Acta. med. Scandinav. supp.* 55, p. 1, 1934.
7. Boje, O.: Die Restredaktion des Blutes in der Ruhe und Während körperlicher Arbeit, *Skand. Arch. f. Physiol. supp.* 9, 11.
8. Smith, F. H., and Smith, K. A.: The Influence of Muscular Exercise on Blood Sugar Concentrations, *J. Clin. Investigation* 16: 289 (May)

9. Personal communication from the Professional Golfers Association
10. Quinlan, John F.: Hypoglycemia in Relation to the Anxiety State and the Degenerative Diseases, *California & West. Med.* 49: 446 (Dec.) 1938.

epinephrine, which results in the acceleration of glycogenolysis in all cells. The glycogen content of muscles decreased appreciably during the action of epinephrine. Thus this combined action of exercise and anxiety results in first a definite increase in blood sugar, followed by a decided fall, resulting in part from an increased liberation of insulin. The latter activity in a foursome coincides therefore with the hypoglycemic symptoms experienced during the period between the ninth and fifteenth holes, or between one and one-half hours and two and one-half hours, and in a twosome between the eleventh and fifteenth holes. The return in the later holes to normal figures is due to glycogenolytic activity of the liver with liberation of dextrose into the blood stream, aided in part by increased hydrogen ion concentration. Studies of metabolic activities of a parallel nature were not performed but it would be interesting to speculate as to the decrease in serum phosphate during this period of blood dextrose depression, as well as lactic acid increase, with correlation of blood pressure readings as well.

From a practical point of view, two suggestions may be made to help combat this period of hypoglycemia: first, a more ketogenic type of lunch, and second, increased carbohydrate intake in the form of sugar or

Clinical Notes, Suggestions and New Instruments

CYCLIC PULMONARY EDEMA AT MENSES IN MITRAL STENOSIS

RELIEF FOLLOWING IRRADIATION OF PITUITARY GLAND

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Acute pulmonary edema in mitral stenosis is not infrequent and may be precipitated by a number of factors. Retention of fluid during the menses is well known and may, among other causes, be due to overactivity of the antidiuretic hormone of the posterior lobe of the pituitary gland. In the vast majority of cases there are few resultant phenomena except an increase in body weight. In the case to be reported, however, advanced mitral stenosis was associated with a marked decrease in cardiac reserve, and serious pulmonary symptoms occurred in each of seventeen successive menstrual periods. Blood studies strongly suggested overactivity of the posterior lobe of the pituitary gland, and the subsequent relief afforded by irradiation of the pituitary gland supports this hypothesis. As far as we are able to determine, no case of a similar nature has been reported in the literature.

REPORT OF CASE

Mrs. B. G., aged 26, was in good health except for slight dyspnea on exertion until the night of Dec. 31, 1937, when while dancing she experienced a feeling of tightness in the chest and throat, a hacking cough and a sense of suffocation. This was followed by a gurgling in the chest and throat which was audible to her husband. The attack lasted until noon the next day and was finally relieved by morphine and inhalations of oxygen. However, the same episode was repeated during the following two days. After several weeks of comparative good health she suffered a series of similar attacks. All the attacks except the initial one occurred at rest and usually during sleep. It was then noted that the attacks occurred only in association with her menstrual period, either immediately preceding the onset or during the period, although they occasionally continued a day or two after the cessation of the flow. Her periods were regular and of normal duration and flow.

She was seen by one of us (J. E.) Nov. 19, 1938, in an attack of acute pulmonary edema with a history of having been awakened from sleep by the symptoms just described. Examination was difficult because of extreme restlessness and cough. Cyanosis was marked, loud bubbling rales were heard throughout the chest, and the heart was extremely rapid, with the typical manifestations of mitral stenosis. The blood pressure was 110 systolic, 80 diastolic. The attack was controlled by two doses of morphine sulfate, each one-fourth grain (0.016 Gm.), within one hour, but the attacks recurred during the next two days. She was admitted to the Mount Sinai Hospital in Philadelphia on November 22, but no further attacks occurred. A blood count showed 82 per cent hemoglobin, 4,280,000 red blood cells and 11,600 white blood cells, of which 70 per cent were polymorphonuclear leukocytes. Except for blood probably incident to menstruation, the urine was normal; blood sugar was 90 mg. and urea 19 mg. per hundred cubic centimeters of blood. The Wassermann reaction was negative. The basal metabolism reading was -11 per cent. The illustrations show the electrocardiogram and the orthodiagram done November 23.

According to the patient and her family, a murmur was heard on routine examination when she was pregnant in 1935, but the lesion was evidently not considered a serious one as activities were not restricted and cardiac studies were not done. There was no history of rheumatic fever, chorea, scarlet fever or repeated attacks of tonsillitis.

In spite of full digitalization, the same violent recurring attacks of pulmonary edema took place at subsequent periods, each requiring one-half grain (0.032 Gm.) of morphine sulfate for relief. Examination of the urine for estrogenic substances

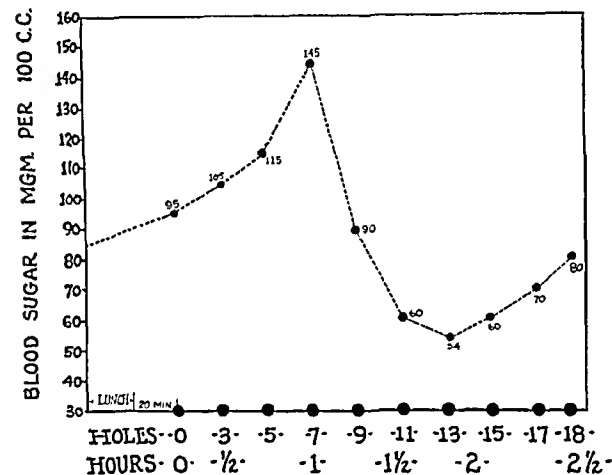


Chart 2.—Composite curve of blood sugar readings in a golf twosome taking two and a half hours to complete. There is an elapsed time of twenty minutes between the end of lunch and starting play.

candy near the eighth hole in a foursome and the ninth hole in a twosome. Following such a regimen, blood sugar levels did not reach such low figures and the players showed fewer signs of fatigue throughout the match.

SUMMARY

Blood sugar studies were made on thirty male golfers ranging from 30 to 45 years of age and possessing handicaps of from 10 to 27.

Following usual luncheons and playing under ordinary conditions, blood sugar dropped to hypoglycemic levels between the ninth and fifteenth holes in a foursome, and between the eleventh and fifteenth holes in a twosome. These periods corresponded to the time of lessened efficiency of the players.

These observations were more pronounced in the more nervous and less accomplished golfers, and less marked in the more able and poised golfers.

More ketogenic types of lunch and consumption of sugar or candy at the seventh or ninth hole resulted in definite decrease in untoward symptoms and, on the whole, better scores.

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From the Edward B. Robinette Foundation, Medical Clinic, of the Hospital of the University of Pennsylvania.

by Dr. Charles Mazer just before the onset of the period in January 1939 showed 3.3 rat units of active estrogen and 6.6 rat units of combined and active estrogen, or about one-fifth the amount usually found premenstrually. Purely from a substitutive standpoint large doses of progynon were given by intramuscular injection, but in February the usual attack of pulmonary edema initiated her period. Because of the possibility that increased blood volume due to water retention incident to menstruation might be a factor in the production of the attack, mercupurin 2 cc. intravenously was given in addition to the morphine. There was a profuse diuresis and, unlike the preceding periods, pulmonary edema did not recur in the succeeding days of this period. The conception of increased blood volume during the menstrual period was subsequently confirmed by blood volume determinations

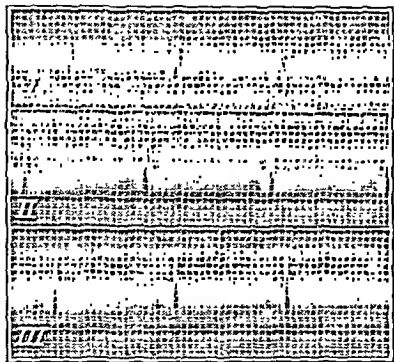


Fig. 1.—Electrocardiogram done Nov. 23, 1938.

done by one of us (J. Q. G.). On March 16, 1939, the blood volume, measured by the method of Sunderman and Austin, was 65 cc. per kilogram of body weight and the melanophore expansion test was negative. Her serum contained no antidiuretic substance for rats. On March 30, during her menstrual period, the blood volume rose to 78 cc. per kilogram of body weight, the melanophore expansion test was positive and her serum contained an antidiuretic substance for rats.

The increase in blood volume and the positive rat and frog tests suggested the possibility of overactivity of the pituitary gland. Irradiation of the pituitary gland in an effort to diminish its antidiuretic effect was suggested, but the patient refused. Castration by means of x-rays or radium was also refused. X-ray examination of the sella turcica was negative.

Thereafter mercupurin was given at approximately weekly intervals but efforts were especially made to give it just before or at the onset of the period. Results were gratifying in that severe attacks of pulmonary edema did not occur, but the patient continued to have a tight feeling in the chest with a hacking cough during her periods. These symptoms were comparatively mild and did not incapacitate her. Several mild attacks of pulmonary edema in the intermenstrual period followed severe exertion, excitement or acute bronchitis.

On June 1 she suffered an attack of pulmonary edema. The menstrual period expected on May 24 was delayed and she had been to a rather hilarious party on the night of May 31. However, she felt well until about 8 p. m. of June 1, when she suffered the severe attack of pulmonary edema. The last dose of mercupurin had been given May 23. This attack was relieved by the usual methods, and menstruation started June 2.

Following this attack the patient consented to have irradiation of the pituitary gland, and 1,132 roentgens was given in eight doses by Dr. Louis Edeiken.

Because the patient was spending the summer at the seashore, injections of mercupurin were continued as a precautionary measure. The menstrual period in July was uneventful and the usual mild symptoms of tightness of the chest and cough were absent. For the first time in seventeen months the patient had not experienced pulmonary symptoms during her period. The menstrual period in August was also uneventful. On returning home in September, the injections of mercupurin were discontinued but the menstrual periods of September, October and November passed without any signs or symptoms of pulmonary congestion. The melanophore expansion test done November 23, the second day of her period, was positive, but the serum contained no antidiuretic substance for rats.

The patient had no further attacks of pulmonary edema but developed mesenteric embolism during an attack of paroxysmal auricular fibrillation on July 6, 1940, and died on July 7.

THE MELANOPHORE EXPANSION TEST

The test as performed for melanophore expanding substance in the blood is as follows: Two frogs of light, well matched color (*Rana pipiens*) are placed in water near a window until the colors are stationary. It is decided which frog is the lighter of the two, and this frog is injected under the skin of the back with 1 cc. of the serum to be tested. The frogs are then watched over a period of twenty minutes. In a positive test the injected frog darkens definitely as contrasted with the control frog.

RAT TEST FOR POSTERIOR PITUITARY OR POSTERIOR PITUITARY-LIKE SUBSTANCE

The rat test for posterior pituitary or posterior pituitary-like substance in the serum is as follows: Adult rats are taken from the cage where dried food and water have been available as desired. Thus they are presumably neither dehydrated nor hydrated. Without anesthesia they are then given 5 per cent of their body weight of water by stomach tube. Immediately thereafter 1 cc. of the serum of the patient to be tested is injected intraperitoneally. The animals are then placed in metabolic cages and the urine passed over one and one-half hours is measured. Complete voiding is insured at the end of the period by beginning the induction of ether anesthesia in the metabolic cage. Under ether anesthesia blood pressure is measured by the indirect method of Griffith. Three animals are used for each test. A rat given normal serum will excrete under the conditions of the experiment about 40 per cent of the ingested water in the form of urine. This allows for a slight but fairly constant loss in the collecting apparatus. After the procedure the blood pressure will not exceed 140 mm. of mercury. A test is considered positive if at least two of the animals excrete less than 10 per cent of the ingested fluid or if one or more develops a definite hypertension.

COMMENT

Generalized or local edema associated with the menstrual periods of normal women has been reported by a number of observers. Heilig¹ and Petersen and Milles² presented evidence to indicate a disturbance of water metabolism associated with the menstrual cycle. The Thorns and Nelson³ observed a gain in weight of 2½ pounds (1,000 Gm.) or more in twenty-four of fifty normal women during the premenstrual period. These investigators demonstrated a retention of sodium, chloride and water during the premenstrual period and intermenstrual periods and an increase in estrogenic substances in the urine during the periods of sodium and chloride retention. No such studies were made on our patient, and the only evidence suggesting water retention is the increase in blood volume noted on the first day of the menstrual period. The single determination of estrogenic substances in the urine premenstrually showed a decrease rather than an increase. It is possible, however, that another mechanism may play a role, for, as Taylor and his associates⁴ remark, "the manner in which estrogens or progesterone may act to prevent sodium excretion can only be guessed at. They may displace sodium into the tissues,

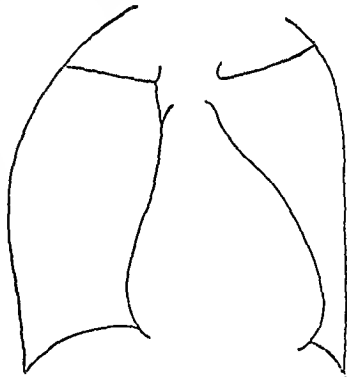


Fig. 2.—Orthodiagram done Nov. 23, 1938.

1. Heilig, R.: Menstruationsstudien: II. Wasser- und Kochsalzhaushalt, *Klin. Wchnschr.* 3: 1117-1119 (June 17) 1924.

2. Petersen, W. F., and Milles, George: Relation of Menstruation to Permeability of Skin Capillaries and Autonomic Tonus of Skin Vessels, *Arch. Int. Med.* 38: 663-681 (Dec.) 1926.

3. Thorn, G. W.; Nelson, Katherine R., and Thorn, Doris W.: Study of Mechanism of Edema Associated with Menstruation, *Endocrinology* 22: 155-163 (Feb.) 1938.

4. Taylor, H. C.; Warner, R. C., and Welsh, Catherine A.: The Relationship of Estrogens and Other Placental Hormones to Sodium and Potassium Balance at the End of Pregnancy and in the Puerperium, *Am. J. Obst. & Gynec.* 38: 748-777 (Nov.) 1939.

prevent its excretion by the kidneys, or act through some other gland, as for example the posterior pituitary." In an investigation of water metabolism of fully matured female pig-tailed macaques whose menstrual cycles varied slightly around a mean of approximately thirty days, Krohn and Zuckerman⁵ noted that the sexual skin of the animal regularly began to swell during menstruation, resorption of the swelling beginning as a rule shortly before the middle of the cycle. The animal's weight fluctuated with the state of the sexual skin and in one case the increase in weight was as much as 18 per cent.

The antidiuretic effect of the posterior lobe of the pituitary gland has been demonstrated in animals. Experimental evidence indicates that the hormone of the posterior lobe of the pituitary gland causes an increased absorption of fluid in the tubules of the kidney and, according to Peters,⁶ the hemodilution that follows ingestion of fluid is exaggerated by solution of posterior pituitary. According to this author the presence or absence of this hormone effects transformations in the elimination as well as in the quantity of urine. Clinically this effect is seen most conclusively in the manner in which solution of posterior pituitary or pitressin checks the functional disturbance of diabetes insipidus.

It is logical to suppose that under certain circumstances the active principle of the posterior lobe of the pituitary gland may be temporarily or permanently increased or decreased. It is claimed by some that lesions of the posterior lobe of the pituitary gland and adjacent portions of the midbrain may cause diabetes insipidus. Conversely, an increased secretion may cause oliguria, as in the patient of Grassheim⁷ with a cystic tumor in the midbrain, in whom the oliguria was relieved by operation. The contents of the cyst, when injected into dogs, had an antidiuretic effect.

In our case the available evidence and mode of relief suggests temporary overactivity of the posterior lobe of the pituitary gland at each menstrual period, with resulting antidiuresis, hemodilution and therefore increased blood volume and, because of the advanced grade of mitral stenosis, pulmonary edema. This is purely speculative, but the increase of blood volume during the menstrual periods and the results following irradiation of the pituitary gland suggest the possibility of the aforementioned sequence of events. Unfortunately, because of lack of cooperation on the part of the patient, records of daily weight and urinary output are not available.

In an effort to demonstrate overactivity of the posterior lobe of the pituitary gland, the melanophore expansion test for frogs and tests for antidiuretic substance for rats in the serum of the patient were performed. In studies as yet unpublished, Griffith, Corbit, Rutherford and Roberts⁸ were able to produce antidiuresis and, in about a third of the animals, hypertension by giving rats 5 per cent of their body weight of water by mouth along with an intraperitoneal injection of 0.12 cc. per hundred grams of body weight of pitressin⁹ diluted 1:150. Hypertension was found not to occur if either the pitressin or the water was given alone. In the technic here recorded 1 cc. of the patient's serum was substituted for the pitressin with essentially similar results. This, of course, does not prove that the substance in the serum was posterior pituitary hormone, but such an explanation appears likely in view of the presence of melanophore expanding substance and the effect of irradiation.

SUMMARY

1. Cyclic pulmonary edema was associated with the menstrual periods of a young woman with advanced mitral stenosis.
2. Repeated attacks of pulmonary edema occurred during fourteen successive menstrual periods. Mercupurin given intravenously during an attack of pulmonary edema prevented subsequent attacks during that period.

5. Krohn, P. L., and Zuckerman, S.: Water Metabolism in Relation to Menstrual Cycle, *J. Physiol.* 88: 369-387 (Jan. 18) 1937.

6. Peters, J. P.: Body Water, Springfield, Ill., Charles C. Thomas, Publisher, 1935.

7. Grassheim, K.: Wasser- und Kochsalzstoffwechsel beeinflussende Stoffe im Liquor bei Erkrankungen des hypophysären Systems, *Klin. Wchnschr.* 11: 1257-1260 (July 23) 1932.

8. Griffith, J. Q.; Corbit, H.; Rutherford, R. B., and Roberts, E.: Unpublished observations.

9. Each cubic centimeter of pitressin (Parke, Davis & Co.) contains 20 pressor units.

3. Injections of mercupurin intravenously, given before the menstrual period, prevented pulmonary edema during three periods, but a hacking cough and tightness of the chest occurred.

4. The patient became entirely free from pulmonary symptoms following irradiation of the pituitary gland and has remained free to date (April 18, 1940), ten months after irradiation).

5. Irradiation of the pituitary was done because examination of the blood the first day of one of the periods showed an increased blood volume and the serum contained an antidiuretic substance for rats and a melanophore expanding substance for frogs.

6. Six months after irradiation of the pituitary gland the melanophore expansion test remained positive but the serum contained no antidiuretic substance for rats.

CASE OF ACUTE POISONING FROM DILANTIN SODIUM WITH RECOVERY

LEON J. ROBINSON, M.D., PALMER, MASS.

Because the complete pharmacology and toxicology of dilantin sodium, recently introduced for the treatment of epilepsy, are still unknown and because there is, as yet, a paucity of reports of acute poisoning from the drug, the following case is recorded.

Dilantin sodium was introduced as an anticonvulsant by Merritt and Putnam¹ and has been reported on by many investigators. The structure of dilantin sodium (sodium diphenyl hydantoinate) is analogous to that of the barbiturates but it is a derivative of glycolyl urea instead of malonyl urea. The mode of action and the intermediate metabolism and excretion are not yet known. The mild toxic effects produced in some cases by poorly tolerated doses of dilantin sodium can be divided into two groups.² The first group is common to phenobarbital and to dilantin sodium and consists of lethargy, ataxia, anorexia, nystagmus and tremor; the second group is characteristic for toxic doses of dilantin sodium and consists of epigastric distress, ocular pain, diplopia, blurred vision and gingival hyperplasia. More serious toxic effects are dermatitis (erythematous, scarlatiniform, morbilliform, exfoliative) and purpuric reactions.

REPORT OF CASE

G. B., a white man aged 25, had epilepsy which resulted from a previous head trauma. His birth and developmental histories were not remarkable. The only illness of note was a severe diphtheritic infection with delirium at the age of 6 years. The family history was negative for neuropsychiatric conditions. At the age of 8 years, when he was running behind a baseball player, he was struck by the baseball bat and rendered unconscious for one hour. He recovered without requiring further care. Since this injury he has had periodic attacks of bifrontal headaches, more marked on the left side. The headaches, unaccompanied by ocular or gastrointestinal phenomena, recur about every three weeks and last all day, unless terminated by acetylsalicylic acid from 10 to 20 grains (0.65 to 1.3 Gm.). His first convulsion occurred nine years after the head injury, when he was 17 years old. Thereafter generalized convulsions recurred at intervals of from six days to four months, despite his taking one-half grain (0.03 Gm.) of phenobarbital three times daily. Because of this complaint he was seen in the outpatient department of the Monson State Hospital May 16, 1939. At this time he had had epilepsy for eight years, the seizures occurring without aura, without any jacksonian features and usually soon after he awakened or with excitement.

The patient was well developed. He was oriented in all spheres, rational, coherent and showed no evidence of hallucinations, delusions or illusions.

The lateral borders of the tongue were scarred. The neurologic and general physical examination were within normal

From the Outpatient Clinic, Monson State Hospital.

1. Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in Treatment of Convulsive Disorders, *J. A. M. A.* 111: 1068-1073 (Sept. 17) 1938; Sodium Diphenyl Hydantoinate in Treatment of Convulsive Seizures *Arch. Neurol. & Psychiat.* 42: 1053 (Dec.) 1939.

2. Robinson, L. J., and Osgood, Robert: Comparative Effects of Phenobarbital and Dilantin Sodium in the Treatment of Epilepsy, *J. A. M. A.* 114: 1334-1336 (April 6) 1940.

limits throughout. The blood pressure was 118 systolic, 82 diastolic. The carotid sinus pressure was normal.

Laboratory examinations showed the following: Urinalysis (four specimens): The urine was amber and acid; specific gravity was from 1.020 to 1.023; it showed a faint trace of albumin and no sugar; examination of the sediment was negative.

Hematology: The hemoglobin was 94 per cent (Sahli), red blood cell count 4,880,000, color index 0.9, white blood cells 8,000, differential count: polymorphonuclear leukocytes 74 per cent, lymphocytes 21 per cent, eosinophils 4 per cent and transitionals 1 per cent. The red cells appeared normal.

Blood Chemistry: Nonprotein nitrogen was 28 mg. per hundred cubic centimeters of blood and uric acid 4 mg.; blood sugar tolerance, fasting 100 mg., one-half hour 120 mg., one hour 100 mg., two hours 100 mg., three hours 90 mg. and six hours 110 mg. per hundred cubic centimeters of blood.

The basal metabolic rate was minus 16 per cent. The Hinton test of the blood gave negative results.

Lumbar Puncture: The initial pressure was 85 mm. of water and the dynamics were normal; 10 cc. of clear colorless fluid was removed and the final pressure was 70 mm.; there were no cells, the total protein was 50 mg. per hundred cubic centimeters of fluid; globulin test negative, and sugar 66 mg.; Wassermann and Hinton tests gave negative results; the colloidal gold curve was 1122222210.

Roentgenogram of skull: Lateral and anteroposterior stereoscopic views showed no abnormality.

The pneumo-encephalogram revealed a normal ventricular system. There were small pools of air in the frontal and temporal areas more noticeably on the left side.

The electro-encephalogram was abnormal, showing during rest waves with a frequency of from 6 to 10 bilaterally, and during hyperventilation additional waves with a frequency of from 3 to 5 from the left hemisphere.

Since the patient continued to have seizures despite the phenobarbital medication, he was advised to take dilantin sodium $1\frac{1}{2}$ grains (0.1 Gm.) morning and night, in addition to phenobarbital $1\frac{1}{2}$ grains nightly. From time to time both he and his mother reported with favorable comments on his incidence of seizures.

On April 15, 1940, eleven months after his first visit to the outpatient clinic, the patient returned with the statement that he had lost two successive positions because of recurrent seizures. He became disheartened and reported that on April 4, 1940, he had ingested forty-five capsules (4.5 Gm. [$67\frac{1}{2}$ grains]) of dilantin sodium. These were taken at 4:45 p. m. At 5:15 he felt extremely drowsy and dizzy and trembled a little. At 5:20 he became unconscious. His mother called the local hospital, which sent its ambulance physician. The latter found the patient in deep coma. The skin was cold and clammy. The pupils reacted to light and in accommodation. The jaws were firmly closed. All the reflexes were reported normal. The pulse was regular, with a rate of 74. Cardiac, pulmonary and abdominal examinations revealed no unusual conditions. All efforts to arouse the patient were futile. Nikethamide 1.5 cc. (25 per cent aqueous solution of pyridine-beta-carboxylic acid diethylamide) subcutaneously produced no effect.

The patient was hospitalized in his home community. Nikethamide 3 cc. was administered intravenously. By this time attempts at gastric lavage evoked struggling on the part of the patient. He vomited small amounts of yellowish mucus. He was given strychnine sulfate (0.001 Gm. [one-sixtieth grain]) and caffeine sodiobenzoate (0.5 Gm. [$7\frac{1}{2}$ grains]). The patient began to move restlessly and continued his aimless movements for one hour and twenty minutes, at the end of which time he regained complete consciousness and was fully oriented. Emesis was induced and the patient vomited 12 ounces (360 cc.) of brownish fluid. The only residual effects noted were severe headache and a strong desire to urinate, accompanied by a sensation of continuous urethral drip. The latter cleared in three or four days, during which time tincture of hyoscyamus 10 minims (0.65 cc.) three times a day was administered.

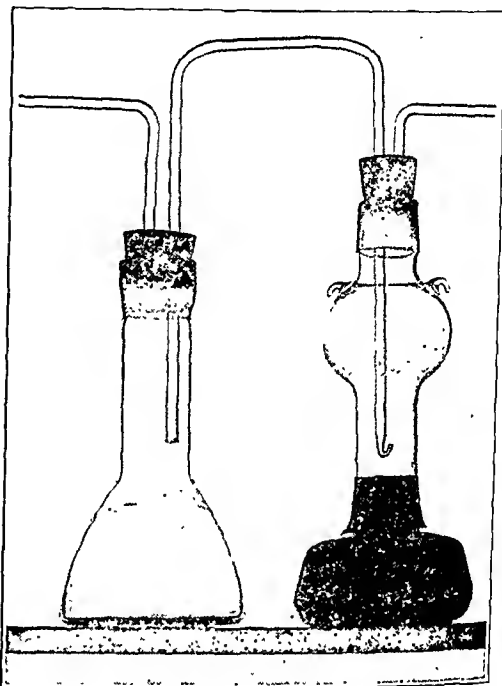
On the fourth hospital day the patient had an epileptic seizure. On the seventh day he was discharged ambulatory and recovered. He was advised to take dilantin sodium 0.1 Gm. ($1\frac{1}{2}$ grains) three times a day. When seen six weeks later he showed no unusual sequelae.

STUDIES IN BLOOD PRESERVATION: THE SHAPE OF THE CONTAINER

JOHN SCUDDER, M.D.; KINGSLEY BISHOP, M.D.
AND
CHARLES R. DREW, M.D.
NEW YORK

Following a preliminary report on the shape of the container as a factor in blood preservation,¹ various flasks have been tested out at the Presbyterian Hospital. A special receptacle² designed with a narrow center section allows the interface forming between the cells and the plasma to settle in the constricted portion. The results, judged by the retardation of both potassium and hemoglobin diffusion from the cells, have been so satisfactory as to lead to its adoption.

If the blood is not used within a week, the supernatant plasma is removed by suction and the plasma stored in the second bottle. Saline solution is added to bring the surface of the



Flasks for blood preservation. The container on the right shows the formation of the interface between plasma and cells in the narrow section of the bottle. The supernatant plasma is transferred into the container on the left by suction.

plasma up into the neck of the flask. This accomplishes a dual purpose. The addition of the saline solution tends to keep the fibrin in solution, and the reduction of the interface retards surface denaturation.

The stability of both blood and plasma is further enhanced by drawing the sample into an atmosphere of carbon dioxide, thereby retarding the formation of ammonia as well as increasing the hydrogen ion concentration.³ This procedure is readily accomplished by flushing out the flask with carbon dioxide and then introducing the blood into the bottom of the container.

These simple factors recommend themselves, as they retard the deterioration of preserved blood.

630 West One Hundred and Sixty-Eighth Street.

This study was conducted under a grant from the Blood Transfusion Betterment Association of New York.

From the Surgical Pathology Laboratory of Columbia University College of Physicians and Surgeons.

1. Scudder, John; Drew, C. R.; Corcoran, Dorothy R., and Bull, D. C.: Studies in Blood Preservation, *J. A. M. A.* 112: 2263-2271 (June 3) 1939.

2. Scudder, John: Shock; Blood Studies as a Guide to Therapy, Philadelphia, J. B. Lippincott Company, 1940.

3. Smith, Margaret E.; Tuthill, Elizabeth; Drew, C. R., and Scudder, John: Studies in Blood Preservation: Some Effects of Carbon Dioxide, *J. Biol. Chem.* 133: 499 (April) 1940.

WESTERN EQUINE ENCEPHALOMYELITIS FOLLOWING
ACCIDENTAL INOCULATION WITH CHICK
EMBRYO VIRUS

REPORT OF A FATAL HUMAN CASE WITH NECROPSY

FERDINAND C. HELWIG, M.D., KANSAS CITY, MO.

A number of cases of equine encephalomyelitis have been recorded as occurring in man. In none of these, however, has the incubation period been established.¹ In 1939 Fothergill, Holden and Wyckoff² reported a case in which equine encephalomyelitis occurred in a woman aged 30 ten days after she was employed in a laboratory, where she worked with chick embryo virus. The route of her infection could not be ascertained although there were rumors of possible injury to a finger from a gold pointed needle breaking off in it. Careful investigation failed to establish the truth of this rumor. No report was made by the patient, although strict orders for reporting the slightest accident were constantly enforced and observed and no damaged needle was turned in.

Since I could not find a single instance in the literature in which the incubation period in the human being was known, the case reported here seemed worth recording.

REPORT OF CASE

On June 16, 1939, about 4:30 p. m., Dr. S., aged 57, a prominent veterinarian, was centrifuging some highly concentrated living chick embryo virus of western equine encephalomyelitis in the vaccine room of his large commercial laboratory. The virus had been placed in the centrifuge and Dr. S. was operating the rheostat. It was the first time the new machine had ever been used. Apparently too much power was applied and the virus was thrown out of the top and all over the lid of the centrifuge. The force was so great that virus was spattered all over the walls and sprayed the windows so that the virus ran in fine rivulets down the window panes. Dr. S. had on no mask or goggles, and even his glasses were covered with the virus. A technician standing near him who was sup-

another screen was placed in the machine and Dr. S. again operated it without mishap. Prior to this date and thereafter Dr. S. was not in the vaccine room and no record of any further contact with virus up to the time of his death could be elicited. On June 30, fourteen days after the accident, he had a very severe headache, which was accompanied by nausea and vomiting. On July 1 his temperature was 103 F. and the nausea, vomiting and headache persisted. His general condition grew

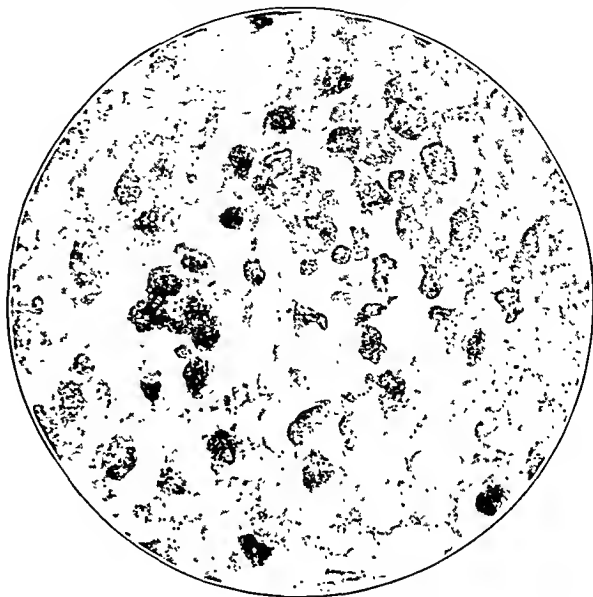


Fig. 2.—Oil immersion view of small focal lesion in the brain. Note preponderance of polymorphonuclear leukocytes and breaking up of ground substance.

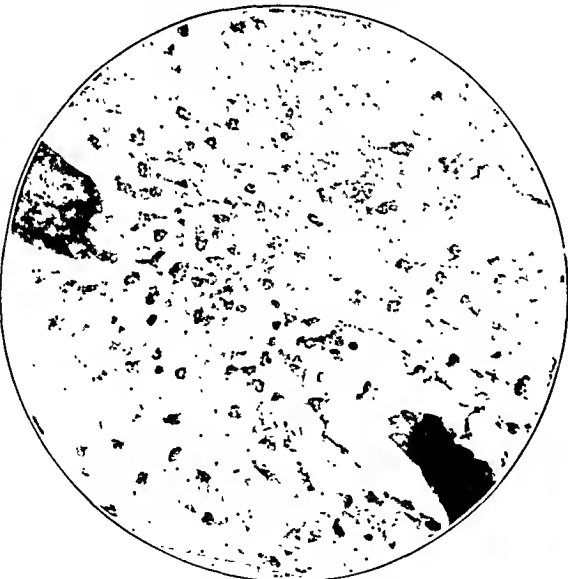


Fig. 1.—Section of minute inflammatory lesion, involving borders of perivascular spaces, under high power.

plied with mask and goggles was also sprayed from head to foot to such an extent that she was forced to wipe both her goggles and her shoes with mercury bichloride solution. Later

progressively worse. Spasticity and athetosis of the upper extremities developed. There was also some spasticity of the lower extremities. He became quite irritable, then delirious and finally somnolent.

On physical examination following admission to the hospital the patient, a moderately corpulent man, was obviously quite sick. No eye signs were present but there was spasticity of the extremities, which was most marked in the arms; and athetoid movements of the hands were quite striking.

On admission his temperature was 103.8 F., his pulse rate 84 per minute. Following admission his temperature ranged from 103 to 105 F. He was given anti-equine encephalomyelitis serum. A severe reaction followed the intravenous administration of the first 200 cc. of the serum, the temperature rose to 107 F. and the pulse rate rose to 140 per minute, shortly followed by a drop of both pulse and temperature to almost normal. Because of his high degree of sensitivity, it was thought, therefore, to employ guinea pig serum, which was tried without reaction. He did not rally, however, and died at 7:30 a. m. July 7, eight days after taking sick.

Laboratory examinations showed a white count ranging from 11,300 to 19,400; the spinal fluid showed 97 white blood cells, of which 92 per cent were lymphocytes and 8 per cent were polymorphonuclear leukocytes; there were 11 red blood cells and the globulin test was positive. The total protein of the spinal fluid was 40 mg. per hundred cubic centimeters one day after entry and the count mounted to 175 white and 134 red blood cells. The color changes shown in the gold curve were 0000110000.

Necropsy.—This was performed forty-five minutes after death. Aside from a terminal left lobar pneumonia, moderate cardiac hypertrophy, a nodular colloid goiter and medullary softening of the adrenals, the chief pathologic changes of interest were confined to the brain. The subarachnoid space contained considerable increase in fluid and the cut surface of the brain appeared unusually moist. The brain weighed 1,620 Gm. On section through the cortex many pinpoint petechiae were seen. The same petechiae were observed in the region of the basal nuclei. Otherwise the brain and spinal cord were not noteworthy.

From the Department of Pathology, St. Luke's Hospital.

1. Olitsky, Peter K.: Infection with Equine Encephalomyelitis Virus, in Brennemann, Joseph: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, 1939, vol. 14, chapter VII, p. 35. Farber, Sidney; Hill, Allen; Connerly, Marion L., and Dingle, J. H.: Encephalitis in Infants and Children, J. A. M. A. 114: 1725 (May 4) 1940.

2. Fothergill, L. D.; Holden, Margaret, and Wyckoff, R. W. G.: Western Equine Encephalomyelitis in a Laboratory Worker, J. A. M. A. 113: 206 (July 15) 1939.

Microscopic Examination: Hematoxylin and eosin, Masson's trichrome, Bielschowsky, Pal-Weigert, Nissl and scarlet red stains were employed on sections from the brain.

The most uniform lesion encountered was the presence of numerous pinpoint accumulations of polymorphonuclear leukocytes admixed with a few monocytes and lymphocytes. In these minute foci there was marked breaking up and fragmentation of the ground substance. Often these tiny infiltrates could be seen abutting directly on the borders of tiny blood vessels. Not infrequently they seemed to arise from these little vessels and involve the wall of such vessels (fig. 1). Practically every section taken from different areas in the brain showed from one to several of these miniature infiltrates, which were usually of such a size that they could often be incorporated in the high power field of the microscope (fig. 2). The next most frequent lesion consisted of pinpoint interstitial hemorrhages of about the same size as the infiltrations, being apparently unrelated to any blood vessel unless it should be a tiny capillary the walls of which had become destroyed. Perivascular hemorrhages and infiltrations of polymorphonuclear leukocytes, monocytes and lymphocytes also were encountered in many sections. Advanced degenerative changes in ganglion cells were also found. The arterioles and capillaries often showed endothelial swelling, and sometimes hyaline thrombi were seen. There was a moderate degree of interstitial edema. At the base and in the medulla the damage was most marked. In some areas of the cortex the pia-arachnoid showed a mild infiltration with polymorphonuclear leukocytes and monocytes. This arachnoid infiltration did not show in many areas. The spinal cord showed only a mild leukocytic infiltration of the pia.

COMMENT

The incubation period following intranasal inoculation with western encephalitis virus in monkeys as carried out by Wyckoff and Tesar³ showed that the temperature peak occurred around the fifth or sixth day following inoculation. This is later than that reached in the eastern disease and the febrile stage in their experiments lasted longer with western infection, although the temperature did not rise as high or fall as precipitately as with eastern virus disease. Moreover, the stage of paralysis developed more slowly in western infection and the comatose stage preceding death was of greater duration than in the eastern disease. These workers were unable to produce the disease by way of the gastrointestinal tract by means of a stomach tube. Dr. Beatrice Howitt⁴ of the University of California has likewise been unable to infect guinea pigs by stomach tube provided no virus is regurgitated back into the mouth. In the horse the incubation period is said to range from one to three weeks.

Our patient was sprayed liberally with the virus on June 16 at 4:30 p. m. and his first symptoms became manifest on June 30, fourteen days after the accident. He died on July 7, eight days after the onset of fever, nausea and vomiting. The gross and microscopic appearances in the brain were more or less typical of equine encephalomyelitis and correspond with the changes observed by other workers. Unfortunately the brain was removed, packed in solid carbon dioxide and sent to Washington, where it was not examined for some time after arrival there. In a communication from the Public Health Service it was stated that the brain was contaminated and that no refrigeration was present on arrival of the material; hence it is not strange that it was impossible to identify or isolate any virus from the brain, since it vanishes very quickly after death.

CONCLUSIONS

A laboratory worker was accidentally inoculated by a spray of highly virulent chick embryo virus of western encephalitis. The incubation period was fourteen days from the time of accidental experimental inoculation to the onset of symptoms. The probable port of entry was through the upper respiratory tract, since the virus was spattered over his face. Careful check failed to reveal any contact with virus for some weeks prior or subsequent to this accidental inoculation.

3. Wyckoff, Ralph W. G., and Tesar, Walter C.: Equine Encephalomyelitis in Monkeys, *J. Immunol.* 27: 329 (Oct.) 1939.
4. Howitt, Beatrice: Personal communication to the author.

Special Clinical Article

SOME RECENT ADVANCES IN VITAMIN THERAPY

CLINICAL LECTURE AT NEW YORK SESSION

T. D. SPIES, M.D.

CINCINNATI

D. P. HIGHTOWER, M.D.

AND

L. H. HUBBARD, M.D.

BIRMINGHAM, ALA.

Long after beriberi, rickets, scurvy and pellagra were recognized and described by physicians, the concept of nutritional deficiency diseases arose. With the development of this concept, a new chapter in medicine came into being. Of late considerable research has been directed toward the isolation and synthesis of so-called accessory food factors, more commonly known as vitamins, and some of these substances have been found effective in the treatment of beriberi, rickets, scurvy and pellagra. The years following the brilliant investigations which led to the isolation, synthesis and clinical trial of thiamine hydrochloride, nicotinic acid, riboflavin, vitamin E, vitamin B₆ and pantothenic acid have, however, been marked by a period of confusion. The literature with regard to these vitamins, and to the deficiencies arising from a suboptimal amount of them, is vast and often contradictory. The problem is so complex and the precise knowledge so meager that we must accept the point of view that a rising curve of complexity is on us. The accompanying illustration shows this complexity. Accordingly, it seems wise to restrict this report to the present status of a few of the therapeutic advances made in the field of nutrition since 1936.

1936: THIAMINE HYDROCHLORIDE

The synthesis of vitamin B₁ (thiamine hydrochloride) in 1936 accelerated clinical investigation and made possible intensive study of the nature and symptomatology of beriberi. Beriberi, in its severe form, affects predominantly the peripheral nervous and the cardiovascular systems. It is characterized by a symmetrical peripheral neuropathy accompanied by degeneration and atrophy of the muscles supplied by the affected nerves, and by cardiovascular disturbances which include edema, cardiac dilatation, speeded circulation, high venous pressure and prolonged electrical systole. The study of many patients with beriberi has shown that they experience a long period of ill health, characterized by prodromal symptoms, before the recognizable symptoms of the disease appear. These prodromal symptoms include loss of weight, strength and appetite, periodic vertigo, burning sensations in various parts of the body,

Owing to lack of space, this article is abbreviated here by the omission of a bibliography which will appear in the reprints.

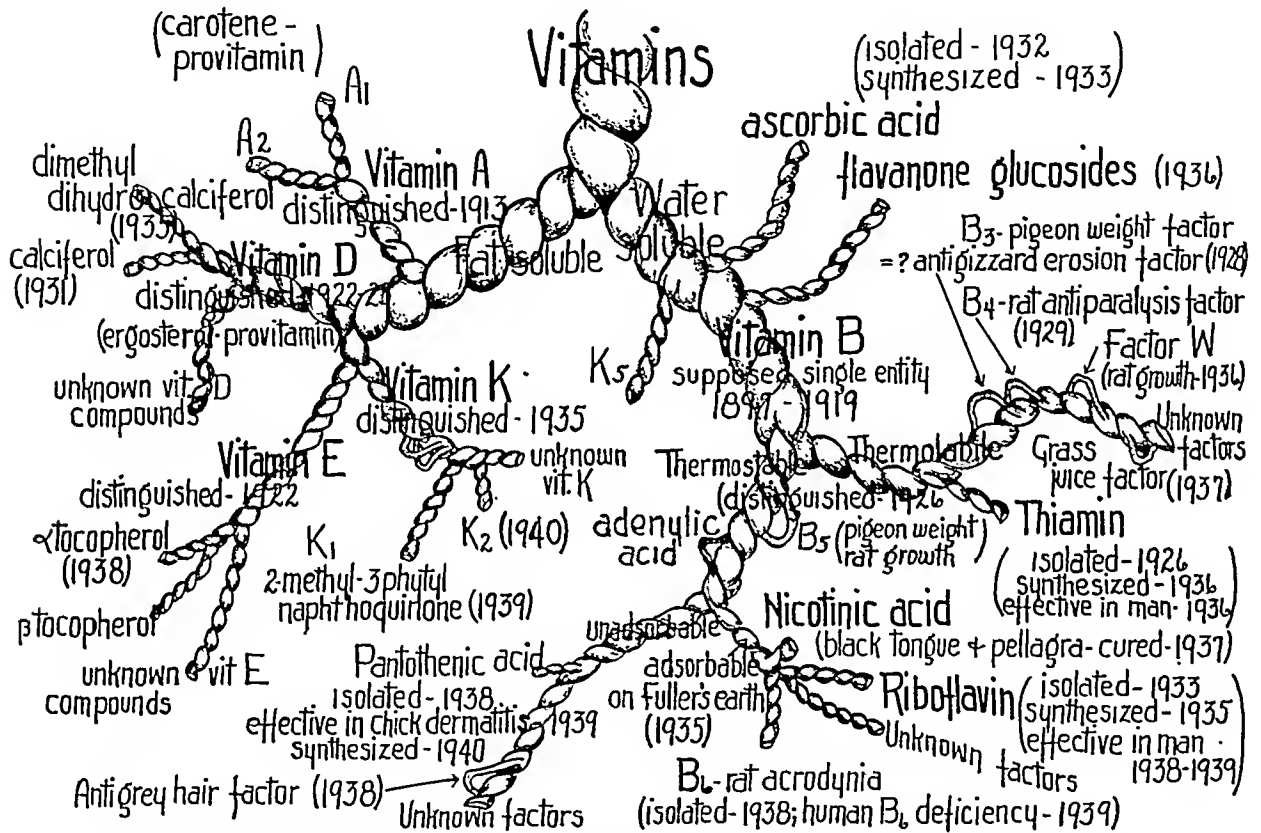
Read in the Medical Division of the General Scientific Meetings at the Ninety-First Annual Session of the American Medical Association, New York, June 11, 1940.

The present paper includes a brief review of the work done by many investigators. The studies conducted by the authors during the past four years have been under the auspices of the Department of Internal Medicine of the University of Cincinnati, the past year, at which time a cooperative project of Preventive Medicine of the University of Texas Faculty of Medicine and the Department of Internal Medicine of the University of Cincinnati College of Medicine was initiated. The heavy expenses of these studies were borne in large part by the John and Mary R. Marile Foundation, the Rockefeller Foundation, the David May Fund, Anheuser-Busch, Inc., Eli Lilly & Co., Mead Johnson & Co. and E. R. Squibb & Sons.

nervousness, numbness, loss of sensation in the extremities, and cramps and tenderness of the muscles.

Vitamin B₁ is of considerable value in the treatment of beriberi and of the acute neuropathy associated with chronic alcoholic addiction, pellagra and pregnancy. Enough information is available to warrant the trial, under controlled conditions, of this substance for persons who have peripheral neuritis associated with dietary deficiency. Vitamin B₁ does not act as an analgesic, and it is our belief that this substance is most useful in the amelioration of the early disorders caused by a deficiency of vitamin B₁. The administration of synthetic vitamin B₁ (thiamine hydrochloride) to persons with acute beriberi relieves the cardiovascular disturbances, induces improvement in response of the

chiefly the alimentary tract, skin and nervous system. Typical glossitis, which is characterized by swelling and reddening of the margins and tip of the tongue and which, as the disease progresses, extends to involve the entire tongue, is one of the earliest symptoms diagnostic of the disease. Stomatitis, gingivitis and pharyngitis also develop and progress in a similar way. These lesions of the mucous membranes are often infected with Vincent's organisms. Nausea, vomiting, ptialism, diarrhea and abdominal distention are usually advanced symptoms of the disease. The dermal lesions of pellagra may occur on any part of the body. These lesions usually are bilaterally symmetrical and are sharply demarcated from the adjacent healthy skin. At first the erythematous area somewhat resembles sunburn,



Diagrammatic representation of the interrelationship of the vitamins. They are schematically differentiated into the water-soluble and the fat-soluble fractions; the latter group is further separated into its thermostable and its thermolabile components. Certain of these substances have been shown to be essential to human nutrition and effective in the treatment of specific deficiency diseases. The physiologic properties of many are as yet undetermined.

muscles innervated by affected peripheral and cranial nerves, restores the normal electrical conductivity of peripheral nerves, relieves gastrointestinal dysfunction resulting from thiamine deficiency, increases carbohydrate tolerance and decreases bisulfite binding substances in the blood. In cases of subclinical thiamine deficiency it often increases the appetite, strength and feeling of well-being and relieves the symptoms arising from early neurologic lesions of beriberi.

1937-1938: NICOTINIC ACID

The isolation of nicotinic acid amide from liver concentrates marks a milestone in our progress in the study of pellagra. Nicotinic acid amide, nicotinic acid, sodium nicotinate, the diethyl amide of nicotinic acid (nikethamide) and other related compounds have been found to relieve many of the symptoms of pellagra. Clinical pellagra is a systemic disease which affects

but later in the course of the disease the color changes to reddish brown, desquamation begins and the underlying skin is seen to be abnormally red and thickened. Permanent pigmentation may develop following frequent recurrences of the dermatitis. In pellagrins, severe mental disturbances, such as apprehension, confusion, disorientation, hallucinations, mania and delirium, are an indication of a very advanced stage of the disease. However, these advanced symptoms are preceded by a period during which the patient complains of loss of weight and strength, lassitude, abdominal pain, numbness, nervousness and forgetfulness. An initial nervous syndrome, characterized by hyperesthesia to all forms of sensation, increased psychomotor drive, anxiety and apprehension with a tendency toward depression, weariness and increased fatigability, headaches and sleeplessness, is typical of this prodromal period. Recognition

of these early symptoms and immediate application of therapy prevents the development of classic pellagra.

The administration of adequate amounts of nicotinic acid, or compounds acting similarly, to persons with acute or relapsed pellagra will cause fading of the fiery red lesions of the mucous membranes and striking improvement in the Vincent's infection associated with it, revive the appetite and restore normal alimentary function, sometimes with a return of gastric hydrochloric acid, increase strength and feeling of well-being, and restore to normal deranged mental functions, provided they result from pellagra and are not of too great chronicity. In cases of subclinical pellagra these synthetic chemical substances will relieve indigestion, diarrhea, burning of the tongue and stomach, burning and itching of the skin, dizziness, forgetfulness, confusion, insomnia and the symptoms of the initial nervous syndrome. Nicotinic acid will also cause disappearance of the abnormal ether-soluble red pigments which are present in the urine of pellagrins, increase the content of coenzymes I and II in the blood and urine and increase the nicotinic acid content of the blood and urine of both normal persons and persons who have a deficiency of nicotinic acid amide.

1938-1939: RIBOFLAVIN

We shall say little about riboflavin deficiency, as Dr. Sebrell has presented most of the essential points. The importance of riboflavin in human nutrition was observed independently by Sebrell and Butler¹ and by the Vilters and Spies.² Lesions at the corners of the mouth (cheilosis) were first described by Sebrell and Butler as a typical manifestation of riboflavin deficiency. Erosions around the eyes and a shark skin appearance of the skin over the nose are also characteristic of a deficiency of this substance. Itching, burning and excessive dryness of the eyes, photophobia, granulation and extreme redness of the conjunctiva, particularly of the lower lids, are rather common complaints among persons suffering from riboflavin deficiency. These conjunctival manifestations are often associated with keratitis.

The administration of riboflavin is followed by disappearance of the cheilosis and "shark skin" lesions of the nose, improvement in general vigor, increase in the sense of well-being, and relief from the ocular symptoms. In addition, it increases the efficacy of nicotinic acid in the treatment of certain pellagrins.

1939-1940: VITAMIN K AND VITAMIN B₆

Vitamin K.—Vitamin K, a fat-soluble vitamin, is essential for the maintenance of a normal concentration of prothrombin in the blood. Animal experimentation and clinical studies have shown that certain hemorrhagic tendencies are due to a low plasma prothrombin resulting from a vitamin K deficiency. Absorption of this fat-soluble vitamin is dependent on the presence of bile in the intestine rather than on the adequacy of vitamin K in the diet. Lowered prothrombin concentration may occur in conditions in which extensive intestinal lesions interfere with absorption or, more frequently, in conditions in which bile is excluded from the intestine by obstruction of the common bile duct. In such cases the administration of vitamin K will restore the normal prothrombin level. Bile salts, of course, must be given along with the orally administered vitamin in cases in

which bile is not present in the intestine; otherwise the vitamin will not be absorbed. Recent work also indicates that newborn infants have a vitamin K deficiency in the first few days of life and that the administration of vitamin K will prevent and cure the hemorrhagic diathesis in at least many cases of "hemorrhagic disease of the newborn."

Pyridoxin (vitamin B₆).—Clinical studies to determine whether vitamin B₆ is essential to human nutrition were undertaken in 1938, soon after the artificial synthesis of this vitamin was accomplished. Spies, Bean and Ashe,³ in a preliminary report, described the favorable symptomatic response to vitamin B₆ by four persons who failed to recover completely when on a selected diet supplemented with thiamine hydrochloride, riboflavin and nicotinic acid. The symptoms responding favorably to vitamin B₆ included extreme nervousness, insomnia, irritability, cramping pains in the stomach, weakness, muscular rigidity, and difficulty and awkwardness in walking. More recently we have treated twenty additional patients with similar results. Vilter, Schiro and Spies⁴ reported that this vitamin, when administered in large amounts, produced a slight reticulocytosis in persons who have macrocytic anemia associated with pellagra or pernicious anemia in relapse. These studies, however, do not imply that vitamin B₆ is an anti-pernicious anemia factor or the extrinsic factor of Castle. Improvement has been noted following the intravenous administration of vitamin B₆ to some patients with idiopathic epilepsy and to persons with amyotrophic lateral sclerosis. One of us (T. D. S.) has seen three cases of myasthenia gravis which showed pronounced improvement within twenty-four to forty-eight hours after the injection of vitamin B₆.

On the basis of the dramatic and beneficial effect of vitamin B₆ in relieving muscular weakness and rigidity, an effort was made to determine whether a similar response would follow its administration to persons with Parkinson's syndrome, a severe lingering disease characterized by tremor of the extremities, weakness, delay of voluntary motion and muscular rigidity. In April of this year Dr. Norman Jolliffe of the New York University College of Medicine reported at a symposium on vitamins at Mount Sinai Hospital, and again before the Minnesota State Medical Association, the effect of vitamin B₆ in relieving the rigidities and weakness in certain cases of paralysis agitans (Parkinson's syndrome). More recently Spies reported before the Illinois State Medical Society the results of studies concerning the use of vitamin B₆ in eleven selected cases of parkinsonism of at least four years' duration, eight of which were arteriosclerotic and three postencephalitic. Within a few minutes there was much improvement in the latter three. Rigidity was decreased significantly and the patients were able to walk without the usual stiffness. Two of the arteriosclerotic patients showed definite improvement, five were unchanged and one was considerably worse. Dr. Jolliffe⁵ has stated that in a study of thirty patients with paralysis agitans he observed "no apparent improvement in the postencephalitic group, little or no improvement in any group of patients hospitalized for over three years and dramatic improvement in approximately 20 per cent of the patients with nonpostencephalitic parkinsonism who had

1. Sebrell, W. H., and Butler, R. E.: Riboflavin Deficiency in Man: A Preliminary Note, Pub. Health Rep. 53: 2282 (Dec. 30) 1938.
2. Vilter, R. W.; Vilter, Sue P., and Spies, T. D.: Relationship Between Nicotinic Acid and a Codehydrogenase (Cozymase) in Blood of Pellagrins and Normal Persons, J. A. M. A. 112: 420 (Feb. 4) 1939.

3. Spies, T. D.; Bean, W. B., and Ashe, W. F.: A Note on the Use of Vitamin B₆ in Human Nutrition, J. A. M. A. 112: 2414 (June 10) 1939.

4. Vilter, R. W.; Schiro, H. S., and Spies, T. D.: Effect of Synthetic Vitamin B₆ on the Hemopoietic System of Human Beings, Nature 145: 388 (March 9) 1940.

5. Jolliffe, Norman: Personal communication to the authors.

been helpless for less than one year." These preliminary observations indicate to the authors that rigidity in some cases seems to be decreased and that vitamin B₆ should have more careful study. It seems likely that some persons with Parkinson's syndrome may have an associated vitamin B₆ deficiency, for indeed it is the close resemblance of the rigidity and awkwardness in walking observed in patients suffering from either disease which prompted us to administer vitamin B₆ to those with Parkinson's syndrome.

Many more studies are necessary before conclusive statements can be made concerning the effect of this vitamin on persons with various diseases. It must be emphasized that a sedative effect of vitamin B₆ may be responsible, in part at least, for the rapidity with which symptoms are relieved and that the administration of this vitamin is warranted only under controlled conditions.

1940: VITAMIN E, YEAST ADENYLIC ACID AND PANTOTHENIC ACID

Vitamin E.—For several years it was believed that vitamin E was concerned specifically with reproduction. During the past decade, however, a definite relationship between an inadequate intake of vitamin E and the normality of the cross striated musculature of the body has been established. Characteristic muscular atrophy occurs in widely divergent animal species when vitamin E is withdrawn from their diets. Restoration occurs following the intramuscular injection of synthetic alpha-tocopherol (vitamin E). During the past year Wechsler⁶ and Spies and Vilter⁷ observed independently that synthetic alpha-tocopherol has a beneficial effect on occasional persons with amyotrophic lateral sclerosis. The injection of 500 mg. of alpha-tocopherol in sterile oil is effective, at least temporarily, in relieving neuromuscular symptoms, roaring sensations in the ears, anorexia, and insomnia of selected persons with malnutrition but without clinical evidence of pellagra, beriberi or riboflavin deficiency. We have observed striking improvement in a few of these people following the administration of vitamin E, but it is difficult to measure objectively the degree of improvement. It would seem that the patients who experience the greatest relief are those who also have some deficiency of vitamin E.

Clinical studies of the therapeutic effect of vitamin E are still somewhat in an experimental stage, and until further work is done the administration of this substance is warranted only under controlled conditions.

Yeast Adenylic Acid.—Adenylic acid is a constituent of the pyridine dinucleotides, coenzymes I and II, and since these intracellular enzymes are fundamental to physiologic processes it was felt that adenylic acid merited consideration for study in the treatment of persons with mixed deficiency diseases. Accordingly, we administered yeast adenylic acid to normal persons and to poorly nourished persons who had symptoms which were not relieved by nicotinic acid, thiamine hydrochloride, riboflavin, vitamin B₆ or vitamin A. The injection of from 3 to 20 mg., dissolved in sterile physiologic solution of sodium chloride, within fifteen seconds produced involuntary, deep, gasping inspiration, fluttering sensation in the upper part of the abdomen and a feeling of fullness in the head. All patients had transient flushing of the neck and face, and the pupils became widely dilated. These symptoms vanished within a few

minutes and left no evidence of a harmful effect. Less intense symptoms of the same type followed the administration of a single dose of 200 mg. of adenylic acid by mouth. Six patients with malnutrition who had intense burning of the oral mucous membranes but no diagnostic evidence of pellagra were relieved following treatment with adenylic acid. The administration of this substance together with nicotinic acid to a series of pellagrins in relapse seemed to increase the effectiveness of the nicotinic acid. However, because of the severe reactions produced by the intravenous injection of yeast adenylic acid we do not recommend its administration to human beings.

Pantothenic Acid.—The structure of pantothenic acid (the chick antidermatitis factor) has been determined and early in 1940 its synthesis was accomplished. Now that it is becoming available for clinical investigation, studies on its relation to the blood, urine and tissues of human beings are in progress. Since there was no information regarding the possible toxicity of pantothenic acid, we administered this substance, under controlled conditions, to a series of normal persons and found that at least 100 mg. may be injected intravenously without producing a reaction or causing a significant change in the blood pressure, pulse or respiration. Spies, Stanbery, Williams and Jukes⁸ observed that the pantothenic acid content of the blood is increased soon after injection but returns to its previous level within twenty-four hours. Stanbery, Snell and Spies⁹ have shown that the pantothenic acid content of the blood of persons having severe deficiency diseases, such as pellagra, beriberi and riboflavin deficiency, is from 23 to 50 per cent lower than in normal persons and that with a rise in the pantothenic acid content there is a simultaneous increase in the riboflavin content of the blood. The patients with an abnormally low concentration of pantothenic acid in the blood have also had less than normal in the urine. These observations suggest that pantothenic acid is important in human nutrition.

GENERAL CLINICAL CONSIDERATIONS OF DEFICIENCY DISEASES

Factors Operating to Produce Deficiency States.—The factors that operate to produce nutritional deficiency diseases are an inadequate intake, increased need, diminished absorption or utilization, or increased destruction or excretion of the essential nutritional substance or substances. Clinical study of deficiency disease syndromes in 3,500 persons, including the 1,500 reported in this paper, has shown that single deficiency states seldom exist. This is not surprising since the dietaries of persons in whom these diseases most frequently occur are deficient in many essential nutrients. The resultant clinical picture is extremely complex; we frequently see evidence of pellagra, beriberi, riboflavin deficiency, scurvy, vitamin B₆ deficiency, vitamin A deficiency and anemia in the same person. The diagnosis of one clinical deficiency syndrome, therefore, necessitates a thorough search for others.

Factors of Safety Operating to Correct Deficiency States.—Certain factors of safety operate to protect the body and to compensate for a deficiency of these essential substances once the deficiency has set in. A wide margin of safety exists between the beginning of a dietary deficiency disease and death from it. We have reported cases in which rest alone was followed by some

6. Wechsler, I. S.: Recovery in Amyotrophic Lateral Sclerosis Treated with Tocopherols (Vitamin E): Preliminary Report, J. A. M. A. **114**: 948 (March 16) 1940.

7. Spies, T. D., and Vilter, R. W.: A Note on the Effect of Alpha-Tocopherol (Vitamin E) in Human Nutrition, South. M. J. **33**: 663 (June) 1940.

8. Spies, T. D.; Stanbery, S. R.; Williams, R. J., and Jukes, T. H.: Unpublished observations.

9. Stanbery, S. R.; Snell, E. E., and Spies, T. D.: Unpublished observations.

improvement and, in certain instances, by healing of the lesions characteristic of a specific deficiency state. More recently we have observed a significant increase in the blood concentration of coenzymes I and II following rest in bed. When treating persons with nutritional diseases, one should therefore curtail their activities as much as possible until restoration of the affected tissue to normal is under way. Another factor of safety is the storage of these essential substances which takes place to some extent in the tissues. Also the body tends to excrete less when a deficiency exists. Nevertheless there is a limit to this self regulation and, if the deprivation of these substances continues, irreparable damage to the tissues will result.

PRINCIPLES OF THERAPY FOR DEFICIENCY DISEASES

General Therapy.—The following general principles of therapy are applicable to all deficiency diseases: Each patient must be considered as an individual problem and treatment prescribed accordingly. A well balanced diet of 4,500 calories, rich in protein, minerals and vitamins, should be eaten each day. The type of food, the mode of administration and the time and frequency of feeding in the more severe cases are dependent on the patient's condition and on his ability to tolerate food. Complete reliance on dietary therapy, however, is not recommended, for the necessary protective substances are present in too small amounts to be effective in cases of well developed deficiency diseases. Furthermore, persons of the lower income group who are most frequently affected by nutritional diseases cannot afford to buy the relatively expensive foods rich in vitamins and protein. Specific therapeutic agents, then, should be given as supplements to a well balanced diet. In the very severe case hospitalization is advisable, for the combined services of a physician, nurse and dietitian are essential. The patient should be kept at complete rest in bed until convalescence is well established. If for any reason the food requirement is increased, efforts must be made to eliminate the cause. Appropriate symptomatic therapy and treatment of coexistent diseases are of course desirable. Treatment in all cases should be based on all the clinical evidence available.

Specific Therapy.—Specific therapy in the form of large doses of synthetic chemical substances induces more rapid and dramatic remission of symptoms of the specific deficiency diseases, shortens convalescence in the severe case, and assures more certain recovery. The indication for therapeutic use of synthetic vitamins and concentrates of yeast and liver is very large indeed, but indiscriminate use is not consistent with the interests of the patient.

Beriberi is treated best by giving pure crystalline vitamin B₁ (thiamine hydrochloride). The administration of 20 mg. a day in 10 mg. doses is recommended for the average case of beriberi in the adult, and for the severe case from 50 to 100 mg. administered in divided doses. Ten mg. daily may be sufficient for the mild case. Infantile beriberi is treated best by giving 5 mg. of thiamine hydrochloride, dissolved in sterile physiologic solution of sodium chloride, twice a day, or 10 mg. by mouth each day. The treatment of the nursing child will be greatly aided by giving the mother satisfactory antiberiberic treatment. Vitamin B₁ may be administered either orally or parenterally, but the latter method is preferred in the acute case because of the greater ease in giving massive doses, the greater certainty of absorption and the more rapid improvement which follows.

Nicotinic acid, nicotinic acid amide and sodium nicotinate are effective in the treatment of pellagra. These substances may be administered orally in tablets or capsules, or parenterally, dissolved in sterile physiologic solution of sodium chloride. The average adult patient will respond to the oral administration of 500 mg. daily, given in divided doses of 50 mg. each, though as much as 1,000 mg. a day may be required in the very severe cases. The parenteral dose varies from 50 to 80 mg. daily, injected intravenously in doses of from 10 to 15 mg. Nicotinic acid amide has an advantage as a therapeutic agent in that it does not produce vasodilatation of the skin or an increase in the temperature of the skin which so frequently follows the administration of nicotinic acid and sodium nicotinate.

From 3 to 5 mg. of riboflavin, administered orally in tablet form or intravenously in sterile physiologic solution of sodium chloride, is effective for the average case of riboflavin deficiency. Since riboflavin is not very soluble in saline solution, the oral method of administration is recommended.

Very little is known concerning either the maintenance requirement or optimal dosage for vitamin K. Early work indicates that maximal prothrombin response is obtained when the crude vitamin extracted from 300 Gm. of alfalfa is given orally over a period of from three to four days. Recent work has shown that the oral administration of from 1 to 5 mg. daily of 2-methyl-1, 4-naphthoquinone usually will give excellent results, though for some cases this amount will have to be increased. Since complete absorption is dependent on the presence of bile in the intestine, it is necessary, when vitamin K is administered orally, to give bile or bile salts along with it, as for example in cases of obstructive jaundice. Satisfactory results are obtained if the daily dose of the vitamin is emulsified in from 1 to 2 ounces (30 to 60 cc.) of bile or is given with a comparable amount of animal bile salts.

The intravenous injection of 50 mg. of vitamin B₆, dissolved in sterile physiologic solution of sodium chloride, is effective in the treatment of symptoms of vitamin B₆ deficiency. Evidence indicates that vitamin B₆ will relieve, at least temporarily, certain other conditions as described in the section on vitamin B₆; but, since response is not uniformly observed in all cases, its use is not recommended until further study has been made.

Vitamin E (synthetic alpha-tocopherol) in sterile oil, injected intramuscularly in dosage of 500 mg., relieves temporarily the symptoms of weakness and pain in the legs. In some cases a second injection of 500 mg. may be required.

Because of the severe reactions produced by the intravenous administration of adenylic acid, its use is not recommended.

Stanbery, Snell and Spies have shown that the content of pantothenic acid in the blood and urine is from 23 to 50 per cent lower in persons having pellagra, beriberi and riboflavin deficiency than in normal persons.

In the mild and moderately severe cases of mixed deficiency disease, dry powdered brewers' yeast (from 75 to 100 Gm.), liver extract (from 75 to 100 Gm.) or wheat germ (150 Gm.) daily should be given orally as supplements to the diet. Yeast and wheat germ have an advantage over the pure chemical substances in that they contain nicotinic acid, vitamin B₁, riboflavin and vitamin B₆, as well as minerals, proteins, enzymes and salts, and probably still other as yet unknown essential factors. A strain of yeast, designated C-50, furnished

by Anheuser-Busch, Inc., for experimental purposes, has been found more palatable than the other strains we have used. Many of the patients who objected to the taste of brewers' yeast will take it without complaint when it is combined up to 25 per cent with peanut butter or catsup.

SUMMARY AND CONCLUSIONS

During the past year and a half, 1,500 persons with clinically associated deficiency disease syndromes have been treated without a death. (The death rate from severe pellagra alone a few years ago was often as high as 54 per cent.) Our studies indicate that these people have a mixed rather than a single deficiency disease, and from a practical standpoint the response of these persons indicates that mixed vitamin therapy is often desirable. We recommend the administration of water-soluble vitamins together, rather than individually, and fat-soluble vitamins together, rather than individually, as having a definite usefulness in the treatment of deficiency diseases. Even when specific therapeutic agents are administered in the treatment of deficiency diseases, persons of all ages should also be given a well balanced, high caloric diet.

Special Article

CONFERENCES ON THERAPY

THE TREATMENT OF BLOOD DISORDERS

IX. POLYCYTHEMIA, HODGKIN'S DISEASE AND SPLENIC DISORDERS

NOTE.—These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments and institutions. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Treatment of Blood Disorders: X. The Disorders of the Blood Produced by Drugs and Their Treatment."

DR. PAUL REZNIKOFF: Polycythemia vera, or erythremia, is due to an increased production of red blood cells. There is not complete agreement as to the cause of this increased production, and the various suggestions which have been made have contributed little to treatment. The aim is either to inhibit production or increase destruction, so that the red blood cells tend to approach normal. Of course there are many ways of doing that, but today I wish to speak only of the four accepted methods of treatment, by which I mean methods that have been tried and found effective and which can be used over long periods of time. Different patients respond differently to the various methods. What is good for one patient is not good for the other, and the customary procedure is to try first the method which the clinic customarily uses and see how the patient reacts to it.

Let us consider first irradiation. The methods vary a good deal. Some workers like to use "spot" irradiation; that is, irradiation of the bone marrow, the spleen or both. That works pretty well. The unitage varies, but commonly 50 roentgens is given at each treatment and the location is varied: at one time over the sternum, at another over the long bones or over the spleen, and so on. Sometimes spot irradiation is used when a patient has pain due either to perisplenitis or to pres-

sure symptoms from a large spleen; but there is not very good evidence that irradiation over the spleen causes much regression of its size or changes the intensity of the symptoms.

Another method is "spray" irradiation. It is effective and well tolerated. We have given as much as 50 roentgens three times a week for from three to six treatments, after which a blood count is taken as a check on the changes produced.

The second method which is used is a hemolytic agent, one which probably has also some depressing effect on the bone marrow, a phenylhydrazine derivative. We believe the least toxic of these is acetylphenylhydrazine. Our usual dose at first is 0.1 Gm. in a capsule. A patient coming in with a count of 10,000,000 red blood cells will be given 0.1 Gm. of acetylphenylhydrazine once a day for about a week; if the patient has to leave the hospital, we usually give this dose every other day. Then we take red blood cell counts once a week, and as the count falls we decrease the dose and try to determine the amount which will maintain a reduced cell concentration and keep the patient comfortable. As a rule patients with polycythemia do not have symptoms from the polycythemia alone. Although each patient is more or less a rule in himself, in general we try to maintain the red cell count at approximately 5,500,000. Actually it is found that some patients will be kept for long periods with a fairly normal count on 0.1 Gm. of acetylphenylhydrazine a week, while others will require this dose every other day.

The third treatment which is effective in polycythemia is solution of potassium arsenite. Those of you who want to get the details of this might read an article by Drs. Forkner, Scott and Wu, published in the *Archives of Internal Medicine* in 1933. There is no question that solution of potassium arsenite will act effectively and can be used over long periods. We have not used it much for polycythemia in our clinic, employing instead a hemolyzing agent, usually acetylphenylhydrazine. We have had good results with that and x-rays, but solution of potassium arsenite will doubtless accomplish the same results, although I think its mechanism is different. It exerts a direct action on the bone marrow and is a regulator of red blood cell formation rather than a depressant. Is that about your point of view, Dr. Forkner?

DR. CLAUDE E. FORKNER: Yes, I think it tends to put cell production up or down.

DR. REZNIKOFF: That is the reason I called it a regulator. We discussed the dosage of solution of potassium arsenite in connection with the treatment of myelogenous leukemia, and its use in the treatment of polycythemia is about the same.

Not one of these three methods of treatment gives immediate relief. It is perhaps ten days or two weeks before the blood count begins to decrease. Some patients have headaches, dizziness and hemorrhages, and it is desirable to do something immediately for those individuals. In such a case there is no better procedure than phlebotomy. Stephens at Rochester studied the question carefully and he believes that phlebotomy at stated intervals does not affect the bone marrow deleteriously; that is, it will neither depress it nor tend to stimulate it. We had a patient who used to come to the hospital from out of town once a month for a phlebotomy, and that is the way he was treated for a period of five years. His blood count remained fairly normal and he felt comfortable. Dameshek, of Boston,

combines phlebotomy with low intake of iron. The rationale for that is not clear. It seems to me that most of these patients have a fairly normal color index and I do not understand why cutting the iron down inhibits cell production because we know that in iron deficiency anemia the red cell count is very often normal.

Those are the four methods of choice and we often combine them. There are questions that sometimes arise: Shall we use polycythemic blood for transfusion? I do, other things being equal. I don't think Dr. Forkner is keen on it, but we have used it several times and so far have not seen any bad results.

There are many other methods for the treatment of polycythemia, but those are the four in most general use. Formerly benzene was used, and I think some people still use it. Perhaps if we did not get such good results with the other methods we would go back to benzene. On the other hand, benzene may also depress platelets and white blood cells, and we want to avoid that. The toxic effects of acetylphenylhydrazine have not been observed in our clinic. The only patient who gave us concern was a man who became markedly jaundiced, and we are not sure but that he had some liver damage to start with.

I should like to emphasize that in addition to treating the blood in polycythemia you must treat the patients. In the first place, these people are likely to have vascular changes and often are high strung, nervous and irritable. They are usually difficult, and you have to treat the emotional factor.

As far as possible you should avoid putting patients with polycythemia to bed, because they are prone to develop thrombosis and it is better to keep them fairly active. These patients also have marked congestion of the mucous membranes, so a diet must be selected which will minimize the possibility of irritating the membranes. I tell them that they should avoid condiments, too much rough food and foods or drinks at too high a temperature. Concentrated alcoholic drinks should also be avoided. These general factors are important.

TREATMENT OF HODGKIN'S DISEASE

DR. FORKNER: Dr. Craver will tell us about the treatment of Hodgkin's disease.

DR. LLOYD F. CRAVER: The great dispute, of course, is as to whether Hodgkin's disease is to be regarded as an inflammatory process or as a neoplasm. I think the general tendency is to regard this disease, at least in its early and intermediate stages, as an inflammatory process, probably caused by various stimuli of the lymph node system, chief among which is tuberculosis. There certainly is much clinical evidence, though perhaps not so much laboratory evidence, that tuberculosis may play a large part in the etiology of Hodgkin's disease. We look on it as a process which gets its beginning as an inflammatory overreaction on the part of the lymph node structures to these various stimuli, whatever they may be, among which the most important may be tuberculosis; a process which, once established, goes on of its own momentum and which in certain cases may go on further to a condition which at least resembles a true neoplasm, Hodgkin's sarcoma.

There is not a great deal to say about the treatment of Hodgkin's disease except to talk about irradiation because, despite the various efforts that have been made along other lines, irradiation remains the chief resource. In many instances it is worth while to treat these patients even in advanced stages, because no matter how bad a case looks you may seem to drag the patient back almost from the brink of the grave by irradiation, pro-

vided you have been fortunate in choosing your doses, the intervals between treatments and the areas treated.

With Hodgkin's disease, as with all the lymphomatous processes, one finds that there is no region of the body that is entirely immune from being involved in one way or another. Therefore Hodgkin's disease and the other lymphomatous processes as well are conditions that should be familiar to all practitioners of medicine, whether they are dermatologists, obstetricians, neurologists or what not. These are some of the main complications that were found in a series of 220 cases: lesions of the lung 29 per cent, pleural effusions 17 per cent, ascites 8 per cent, jaundice 6 per cent, itching 29 per cent, various cutaneous lesions 13 per cent, various neurologic lesions 12 per cent, lesions of bones 18 per cent. I firmly believe that all those complicating symptoms and lesions would give a higher percentage if we had followed all the 220 cases all the way through. Lesions of the bone, for example, which are detectable roentgenographically I believe might be found under modern conditions in perhaps as many as 45 or 50 per cent of all cases of Hodgkin's disease. Under modern conditions of radiation therapy, when the patients do not die of mediastinal pressure or other features from which they perhaps did die years ago they are possibly kept alive long enough to have more of these complications. As for the neurologic lesions, you will find in the literature cases in which operation has been performed for supposed primary spinal cord tumor, the operation revealing Hodgkin's disease, which was not primary there but gained entry to the spinal canal along the intervertebral foramina.

Hodgkin's disease may produce lesions in the lung simulating sarcoma metastases. In general, when a patient with Hodgkin's disease has that amount of lung infiltration the outlook is pretty bad; yet at times it is possible to clear it up satisfactorily, at least temporarily, by irradiation. We have had several cases in which a lung abscess has formed apparently as a result of bronchial blockage and retention of secretions and breaking down of lung tissue, and two instances of tracheo-esophageal fistula.

As an illustration of another type of intrathoracic Hodgkin's granuloma, I might cite a young woman presenting a bulky intrathoracic mass filling one side of the chest. Looking at her chest film, one might think the mass grew out from the mediastinum or at least from lung infiltration, but after irradiation there was a residual nodule on the inner surface of the chest wall, and spot films of the ribs showed that three or four ribs were grossly involved by an osteolytic process. This patient survived about six years after the disease began. She had about every conceivable complication. At one time she had complete paraplegia below about the ninth dorsal level. She could not even wiggle her toes. That was after she had been under treatment for two years. Heavy irradiation given promptly over the appropriate level in the spine resulted in her being able to walk within a month or six weeks, and she was up and around for two years after that before her terminal state.

The type of bone involvement most commonly seen complicating Hodgkin's disease is an osteolytic process, often found in ribs, sternum, vertebrae, pelvis, humerus or femur. A more uncommon type of bone lesion in Hodgkin's disease is the osteoplastic variety, likely to involve more than one bone especially vertebrae, pelvis and femurs. In some cases one bone, as a single vertebra, may show osteoplasia. This type of lesion is usually accompanied by rather vaguely defined pairs

over a large field about the involved bones, and it may be relieved, at times very well and at other times less satisfactorily, by irradiation. I think that in general the osteoplastic type shows less relief from pain after irradiation than does the osteolytic type.

Often it is difficult to tell whether one is dealing with a little variation in the roentgenographic technic or an actual osteosclerotic process. Blood phosphatase levels seem to be fairly well correlated with the bone lesions, especially in Hodgkin's disease, although not too closely. There are very high phosphatase levels, in some cases up to 35 and 40 units per hundred cubic centimeters (Bodansky).

A rare condition is ulcerating Hodgkin's granuloma in the skin. The girl I mentioned who had the massive chest involvement and paraplegia had a cutaneous granuloma behind her left ear simulating a sebaceous cyst. It did not contain pus on incision and cleared up promptly after a single low voltage roentgen treatment.

Now there are many different principles used in the irradiation of Hodgkin's disease. Some like to use large doses, some like small doses; some like to irradiate large fields, others prefer small fields. I think there is a certain scope for total body irradiation in Hodgkin's disease. The general practice among most roentgenologists in giving local irradiation is to use a fairly small dose at a time, not over 100 or 200 roentgens. Some years ago we were in the habit of using rather large doses, in the order of from 400 to 600 roentgens at a single exposure, and we have the impression that some of our patients that have done the best have been those treated by that method. I do not think that we would want to put ourselves in the position, however, of recommending large doses, singly or repeated a few times, as the routine method. I think the treatment in Hodgkin's disease has to be greatly individualized. As an example of the method of heavy doses at a sitting, a patient treated in 1931, whose disease was limited apparently to each side of the neck, never had any evidence of mediastinal involvement or generalization of the process. We treated his neck repeatedly by heavy single doses of about 400 or 500 roentgens at intervals of three or four weeks. He now has some radiation changes in his skin and a certain amount of atrophy and dryness but no breaking down. He has been working continuously and is in excellent condition at the present time, with complete regression of the disease.

Our proved cases of Hodgkin's disease show a five year survival of 17 per cent, a figure considerably lower than that reported by some workers. Gilbert in Switzerland reports 34 per cent five year survivors, but I feel that his patients must come to him in considerably earlier stages on the average than ours do because a great many of our patients who have been treated a good deal elsewhere are sent to us as difficult problems. I believe that for 17 per cent to survive five years is not bad considering the type of cases we receive.

As far as other methods of treatment are concerned, transfusions are of value to put the patient in better physical condition so that he may tolerate further irradiation. Iron is also of value at times. It is important to have the patient carry out a regimen as for tuberculosis, with rest and fresh air, moderate exposure to sunshine and a good nutritious diet. Other than that, there is not much to be done.

The problem of itching becomes troublesome at times. It is best relieved by treating the active Hodgkin's disease if you can find it. A patient whom I first saw about

a year ago had a bulky mediastinal mass. Biopsy of a neck node showed a rather active type of Hodgkin's disease, almost Hodgkin's sarcoma. She had such severe itching that she was covered literally from head to foot with long deep scratch marks. She had been treated by a dermatologist and had been seen in consultation by a hematologist, who advised against treating the mediastinal mass, apparently because he believed that it was so active that it might be aggravated by treatment or that she was going to die soon anyway; but she did not die. She fussed along for a year, getting a little roentgen treatment for the skin and various salves and lotions with no benefit. I decided to ignore the skin condition but to irradiate the mediastinal mass. Within three weeks the itching stopped entirely. The skin lesions cleared up after a few months, and she has gained about 20 pounds (9 Kg.). So the principle in treating itching is to find the active Hodgkin's disease and treat that. The various dermatologic measures do not do much good.

DISORDERS OF THE SPLEEN

DR. FORKNER: The treatment of some splenic disorders is discussed by Dr. Andrus.

DR. WILLIAM DEWITT ANDRUS: Splenectomy has come to be a well recognized part of the treatment of certain disorders of the blood and blood forming organs, notably congenital hemolytic jaundice, thrombopenic purpura and Banti's disease, although we must admit that both the role played by the spleen in the production of these disease pictures and the exact factors which bring about improvement after its removal are not clear.

Congenital hemolytic jaundice, representing the purest type of chronic hemolytic anemia due to intrinsic factors, is characterized by increased fragility of the red cells in hypotonic salt solution and by spherocytosis, reticulocytosis, splenic enlargement and a positive indirect van den Bergh reaction.

In the light of present knowledge of the role of the spleen in the destruction of red cells its removal would seem definitely indicated in this condition, in which the cells are abnormally fragile. It should be remembered, however, that the destruction of red blood cells is a function of the reticulo-endothelial system, in which the spleen plays a dominant role because of the concentration of a large portion of the elements of this system in that organ. By removing the spleen, therefore, we remove only a portion of the cells responsible, but fortunately a sufficient portion to restore a more nearly normal balance between blood formation and blood destruction in most cases.

In a typical case the indications for splenectomy are obvious and overwhelming, and the question resolves itself into selecting the optimum time for operation. As a rule it may be said that one should avoid operation when the patient is going into a hemolytic crisis and perform splenectomy as the crisis is receding or in a free interval. This is not always possible, however, as the crises may be very severe or recur so frequently as to leave little choice. In general the patients stand the operation well, as the spleen, though often much enlarged, is seldom adherent and can usually be removed quite easily.

More debatable is the question of splenectomy in patients who have the disease in a latent form, many of whom undoubtedly may go on for years or even throughout life without showing acute symptoms. Such patients should be kept under close observation, and operation should be advised if any tendency to abnormal hemolysis is noted, as even a very long period of free-

dom from symptoms is no guaranty of their continued absence. In one of our patients acute symptoms developed at age 58, including anemia with a count of 1,600,000 red cells but fortunately with a very high reticulocyte count. She stood operation well and has made an uneventful recovery.

The results in the eighteen cases of familial hemolytic jaundice in our series have all been good. There have been no operative deaths, and with the exception of one patient who died of pneumonia after four years and a boy in whom portal thrombosis developed three months after operation, all are living and well.

Thrombocytopenic purpura, of which there were fourteen cases in our series, is characterized by purpura, spontaneous hemorrhages and a marked decrease in the number of platelets in the circulating blood. The bleeding time is prolonged and the clot shows poor retraction. Changes in capillary permeability also play a role. The suggestion has been made that the disease really involves the entire reticulo-endothelial system.

Splenectomy is now recognized as indicated and gives excellent results in the typical cases associated with definite thrombopenia. However, the high mortality in the acute cases in the earlier reported series—as high as 87 per cent in some reports—compared with the apparent safety of the operation in the chronic type of the disease led surgeons and internists alike to condemn splenectomy in the acute stage. This mortality has been steadily falling, however, and some of the most brilliant results have followed early operation. However, it must be said that patients with the disease in the acute form are not good operative risks, and that fact will deter surgeons from operating on them except as all other measures fail.

Various medical measures, particularly repeated blood transfusions, may arrest the hemorrhage or even bring about an enduring remission of the disease in some cases, and the injection of ascorbic acid is sometimes capable of producing remarkable improvements or remission. However, in many cases even these measures fail to stop the bleeding entirely or to restore the blood picture to normal, and they but rarely produce the really spectacular results which often follow operation.

There were no deaths from the operation in our group, although one patient died five months after operation with persistent thrombopenia and anemia. It is possible that we were mistaken in our diagnosis and that she should have been classified as having aplastic anemia. Another patient died with agranulocytosis precipitated by aminopyrine three years after splenectomy. All the remainder are well and have practically normal red cell counts from six months to four and one half years after operation. The platelet counts are known to be normal in all except one, who has not been back to the follow-up clinic. She writes, however, that she is free from her symptoms. One patient had a high platelet count at the time of the last observation.

With regard to Banti's disease (splenic anemia), although Greisinger is said to have used the term "splenic anemia" in 1866, it was Banti in 1883 who first gave impetus to the study of this condition, and Osler from 1900 to 1902 added to our knowledge of the clinical picture. Banti described the disease as characterized by progressive splenomegaly, anemia of the microcytic type, leukopenia, slight thrombopenia and hematemesis, progressing to obvious cirrhosis of the liver with jaundice and ascites. He also considered phlebitis of the portal vein as a uniform feature of the

disease. There is doubt as to whether the primary disease is in the spleen or the liver.

The removal of the spleen in this condition seems definitely warranted in the early stages and may alleviate some of the symptoms over a considerable period. The benefit which results would seem to be due to the reduction of the amount of blood coming to the liver through the portal vein which follows splenectomy. However, the operation is attended with certain risks, since the spleen is commonly adherent and has developed a collateral circulation at its upper pole which may be difficult to handle. Further, in many of the patients the platelets reach very high levels after operation and thromboses are not uncommon. Indeed, if one accepts the criterion of an unexplained febrile course as possibly indicating thrombosis, this complication would seem to be quite common in this disease.

There were no operative deaths in our series of ten cases, but two years after operation one patient died of progressing cirrhosis with ascites. The longest time which has elapsed since operation is three and one half years, and three additional patients have suffered recurrence of hemorrhage.

In general, the operative mortality is higher in this condition than in either of the foregoing and the results less satisfactory. Pemberton reports 167 splenectomies for this condition with sixteen deaths. The remaining 151 patients were followed for as long as twenty-two years, and fifty-two of them had died—more than one third from recurrence of hemorrhage. Similar study of 118 operations for hemolytic jaundice showed four operative deaths and only seven additional fatalities occurring during the follow-up period.

COOLEY'S ANEMIA

We have performed splenectomy in six cases of Cooley's anemia—the peculiar anemia of childhood which occurs apparently only in children of Mediterranean parentage. The youngest was less than 6 months and the oldest 6 years of age. There were no operative deaths, but two of the patients have since died, one eight months and one two years after operation. There is no evidence that splenectomy cures the condition, and the best that can be said is that the patients seem somewhat improved.

In conclusion it should be said that the results of splenectomy in congenital hemolytic jaundice and thrombocytopenic purpura as well as in selected cases of Banti's syndrome amply justify its use but that attempts to expand the indications beyond these three conditions are fraught with danger and in addition give very poor results for the most part.

DISCUSSION OF QUESTIONS

DR. FORKNER: First, I should like to ask Dr. Reznikoff what he considers to be the polycythemic level of red blood cells. We frequently find patients in the wards with counts of 5,500,000, of 5,800,000 or even of 6,000,000, and one immediately jumps to the conclusion that this is polycythemia vera.

DR. REZNIKOFF: In general if a male patient has a count under 6,000,000 and no symptoms, we don't pay much attention to it in our laboratory, especially if the hematocrit reading is normal. If the count is between 6,000,000 and 7,500,000, we usually term that an erythrocytosis analogous to leukocytosis. There should be very few symptoms as a result of an increase up to 7,000,000 or 7,500,000. Above 7,500,000, especially with a concomitant increase in the hematocrit level, we speak of erythremia, which is analogous to

leukemia and is more likely indicative of polycythemia vera. Of course, we see patients with polycythemia vera, as judged by later counts, who have a normal number of red cells, especially those who have been treated, so we cannot make the diagnosis of the disease on the basis of the blood count alone.

DR. FORKNER: Normal males not infrequently have blood counts as high as 6,000,000.

DR. HARRY GOLD: Theoretically, it would seem to me that arsenic, if it is effective, might be more desirable than phenylhydrazine because, as I understand, arsenic suppresses the red cell formation whereas phenylhydrazine exerts its action by destruction of red cells. The products of destruction of red cells produce undesirable effects. I believe that the kidneys sometimes rebel against some of the decomposition products. The tubules get into trouble.

DR. REZNIKOFF: I think that our patients, some of whom have been treated for eight and nine years with acetylphenylhydrazine, do not show evidence of damage to either the liver or the kidneys. They are able to work without difficulty.

DR. FORKNER: With further reference to the use of arsenic I might say that this substance will bring a red count down from almost any level to normal. It is difficult to push the count below normal with arsenic, but on the whole it is more difficult to get a satisfactory response with solution of potassium arsenite than with either x-rays or phenylhydrazine. In choosing an agent for treatment I would put solution of potassium arsenite as third choice. We employed it because we were interested in the mechanism of the effects of arsenic. We found that it works in pernicious anemia, in polycythemia and in leukemia. Just how it works we do not know, but it does depress the bone marrow. On the other hand, phenylhydrazine stimulates the leukopoietic tissue of the bone marrow.

DR. GOLD: Is it stimulated by the phenylhydrazine directly or by the products of the destruction of red cells?

DR. REZNIKOFF: There is evidence of a stimulation of the leukocytes even without treatment. The disease itself causes a stimulation.

DR. FORKNER: But they go higher with phenylhydrazine, don't you think?

DR. REZNIKOFF: That is true in a certain number of these patients; some go over into leukemia.

DR. FORKNER: There is another point in connection with the use of phenylhydrazine in polycythemia, and that is it may cause thrombosis, particularly in older patients. It is a capillary toxin.

DR. REZNIKOFF: Has that been your experience?

DR. FORKNER: Yes.

DR. REZNIKOFF: We find the incidence of thrombosis just as high in untreated patients.

DR. McKEEN CATTELL: To the extent that these conditions occur in children, I wonder whether they present special problems in treatment. Cooley's anemia, mentioned by Dr. Andrus, belongs to this group.

DR. CARL H. SMITH: A problem that has come up recently concerns the adequate treatment of Cooley's anemia. The separation of erythroblastic anemia from the miscellaneous group of von Jaksch's anemia by Cooley has brought to light many children suffering with this disease. As pointed out by Dr. Andrus, Cooley's anemia with few exceptions is limited to children one or both of whose parents were born in Mediterranean countries, especially Italy, Greece or Syria

and most frequently Sicily. For that reason the designation Mediterranean anemia or thalassemia has been suggested by Whipple and Bradford. The outstanding characteristics of this disease are not alone its racial but also its familial tendencies, the skeletal changes and the appearance of large numbers of circulating normoblasts. Undoubtedly the disease is transmitted as a recessive characteristic, but no instance has as yet been recorded of its transmission by an adult with the active form of this disease. While severe cases begin in early infancy, milder cases pass unrecognized until later childhood. There is evidence that, like hemolytic jaundice, the disease may be latent in healthy members of the family so that inheritance is a possibility. It is also possible that in this country there are many with mild or latent forms of this disease who may perhaps be suffering with an unexplained low grade chronic anemia.

The child with the active form of this disease shows a pronounced splenomegaly, a lesser degree of liver enlargement, frontal and parietal bossing, prominent malar eminences, slanting eyes, a muddy yellow complexion and icteric scleras. All these features combine to give these children a mongoloid appearance and account for the well known resemblance of the affected children to one another rather than to their normal sisters and brothers.

The blood shows a moderate to severe anemia, leukocytosis, reticulocytosis, an elevated icteric index, numerous nucleated red cells, which are remarkably increased following splenectomy, and a striking resistance of the red cells to hypotonic saline solution in fragility tests. X-ray study of the skeletal system reveals the evidence of the extreme hyperplasia of the bone marrow by osteoporosis, thinning of the cortex, trabecular atrophy, and thickening of the skull which is first observed in the frontal bones. Lateral views of the skull show an enlarged diploic space which is either finely granular or mottled, or striated, the latter giving the appearance of hair standing on end.

With the earlier recognition of the condition by the roentgenogram, blood studies and its suspected recurrence in an affected family, we now have under observation in our clinic a fairly large group of infants and young children with this disease. The problem with which we are confronted is what procedure to follow, not in the moderate or advanced cases that come to you, Dr. Andrus, for splenectomy, but for the mild and early cases we have been able to uncover. Should splenectomy be reserved for cases in which the weight and pressure effects of the greatly enlarged organ seriously inconvenience the child, or should the spleen be removed when the disease is first recognized, before it has become large, before the liver undergoes enlargement and before extensive skeletal changes set in? It is entirely probable that splenectomy prolongs life, and this is strikingly illustrated by the patient of Stillman and Hitzrot, who lived eighteen years after the operation. We are now following a small group of infants on whom splenectomy was performed in early infancy. While it is too early to arrive at any conclusion, splenectomy seems to have retarded the disease, but the choice of cases and optimal period for this operation await further study.

Since the disease is only in part hemolytic and is probably due fundamentally to a deficiency of unknown hemopoietic principles or to a metabolic disturbance, splenectomy can be expected to modify the disease but slightly. Where the hemolytic activity is extreme, however, splenectomy is most beneficial. In our experience

one of the prime benefits of this procedure has been the reduction of the number of transfusions required to maintain life. It is often difficult to obtain and transfuse blood at biweekly intervals, as is sometimes necessary in the severe cases in infants and young children. In some of our cases in which this need existed, splenectomy has succeeded in lengthening the interval between transfusions. We are endeavoring at present to determine the level at which children with this disease can live comfortably without transfusion.

DR. HENRY B. RICHARDSON: Can you tell whether this is an anthropologic group or a geographic group?

DR. SMITH: We know little about the anthropologic aspect of this disease. At present it cannot be stated whether there is any one race which possesses this recessive character. While with few exceptions this disease is limited to children of Mediterranean parentage, it has been pointed out by several observers that inhabitants of these countries represent an admixture of races. During the reign of Alexander the Great, for instance, the Greeks colonized the Mediterranean countries extensively, and it has been shown that the southern Italians with this disease are in part of Greek origin. Caminopetros in Greece has recently pointed out that some of the settlers about Athens have originated from Asia Minor and that they represent a mixture of many races with the Mongolian. Among the parents and grandparents of children with erythroblastic anemia, he has observed individuals with characteristic Mongolian eyes. It should be emphasized, however, that the Mongolian appearance of these children is in reality produced by skeletal changes in this disease.

DR. CRAVER: Have you found any in the Negro race?

DR. SMITH: I know of no instances of this disease among Negroes.

DR. ADE T. MILHORAT: Does roentgen treatment influence the bony lesion?

DR. SMITH: X-rays do not modify this disease. There is no specific treatment for it. Iron, copper, liver, extracts of glands and of other organs, and vitamins have been employed without success. At the suggestion of some observers that the disease may represent a congenital form of malaria, we have employed quinine, but again without results.

DR. FORKNER: Excessive irradiation can produce purpura.

SUMMARY

DR. GOLD: The diagnosis of polycythemia vera does not depend on the blood count alone. However, symptoms are likely to appear at red cell count levels of about 7.5 million, especially when the hematocrit is increased. The more specific measures in treatment are directed to the reduction of the red cell count. This is achieved most rapidly by phlebotomy, which gives immediate relief from such symptoms as headaches, dizziness and hemorrhages. Acetylphenylhydrazine appears to be the most effective chemical agent for reducing the red cell count. Its mode of action is to destroy red cells in the circulation. Arsenic in the form of Fowler's solution may also restore the red cell count to normal, but it is generally less effective than acetylphenylhydrazine in polycythemia vera. Its mode of action is different and appears to be through an influence on the erythrogenic function of the bone marrow rather than by destruction of red cells. Reduction of the red cell count in polycythemia vera may also be accomplished satisfactorily by irradiation, which may be applied either by the spot or by the spray method.

With regard to Hodgkin's disease, the view has been expressed that in the early stages it is probably an inflammatory process in the lymph node system, which later acquires a growth momentum of its own. Practically every system of the body may be involved in Hodgkin's disease, giving rise to lesions in the lungs, pleural effusions, ascites, jaundice, itching, cutaneous lesions, neurologic lesions and involvement of the bones. The treatment of Hodgkin's disease is essentially a matter of suitable irradiation. The lesions are quite sensitive to radiation therapy and marked improvement is often obtained in some of the most advanced and seemingly irreversible stages of the disease with appropriate treatment which involves suitable doses, intervals and areas of application. The details of the use of irradiation in this disease, which have been discussed by Dr. Craver, need not be rehearsed. Suitable radiation therapy not only causes the lymph node masses to diminish in size or to vanish but improves the patient's general health. One instance of severe pruritus was cited in which the treatment of the mediastinal masses resulted not only in their disappearance but in the cessation of the intractable itching.

We have had a brief account of the use of splenectomy in disorders of the blood and blood-forming organs. It appears to be an effective therapeutic measure in the relief of congenital hemolytic jaundice, thrombocytopenic purpura, Banti's disease and possibly Cooley's anemia. Dr. Andrus and Dr. Smith have outlined the essential differential characteristics of these diseases and the indications for splenectomy.

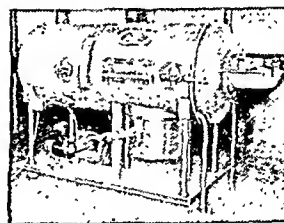
Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

COLUMBIAN RESPIRATOR ACCEPTABLE

Manufacturer: Columbian Steel Tank Company, 1401-1621 West Twelfth Street, Kansas City, Mo.

The Columbian Respirator produces artificial respiration simulating natural breathing for indefinite periods of time. The respirator applies a new principle for controlling vacuum and pressure which is described as a "liquid sealed air pump."



Columbian Respirator.

A cylindric steel chamber containing a removable bed is mounted on a framework, which also supports the operating mechanism. A one-sixth horse power motor operates the unit on direct or alternating current. It is possible to obtain within the chamber a maximum positive pressure of 15 cm. and a maximum negative pressure of 15 cm. The respirator is 56

inches high, 80 inches long and 32 inches wide, and the shipping weight is approximately 1,300 pounds.

The chamber of the respirator is available on the one side through three 5 inch diameter rubber sealed hand ports, and on the other through two hand ports and one bedpan door 6 inches wide by 16 inches long. The interior is illuminated by an electric light. On each side of the respirator is a chrome framed viewing window made of unbreakable cellulose acetate. The bed assembly is supported on large roller casters so that it can be pulled full length out of the respirator shell. The bed frame is hinged and a hand screw outside the respirator permits raising and lowering the patient's shoulders. A

mattress made with "kapok" filler and transparent waterproof cover is standard equipment.

In operation, the patient is placed on the bed, which is extended full length out of the shell, a sponge rubber neck seal is pulled over the head, and the bed is rolled into the respirator. Two hand screws are tightened, and the patient's body is sealed within the chamber. The head remains outside the respirator, lying on a pillow, which is supported by an adjustable canvas swing which can be raised or lowered by removable solid arms. The neck seal is held in place by a self-centering neck ring and three hold down clamps.

The liquid sealed air pump, a feature of the mechanism, consists of two telescoping tanks. A chrome tank, open at both ends, is bolted to the body of the respirator and fits within another tank of stainless steel which holds a narrow ring of liquid, preferably a solution of water and glycerin. A rocker arm raises and lowers the outer tank, creating a liquid sealed vacuum in the stationary inner tank; this results in a movement of air in and out of the body of the respirator. The alternate vacuum and pressure causes the chest to rise and fall as in normal breathing. In clinical use it was reported that the pump was quiet in operation. The volume of vacuum and pressure is controlled by inlet and outlet valves of the body of the respirator, and an adjustable arm permits the length of the piston stroke to be changed. A speed changing pulley provides a range of from ten to thirty respiration per minute with a number of graduations. An auxiliary hand drive is provided for use in case of power failure or when electric power is not available. Operating the respirator by hand is automatic except for counting the number of crank turns per minute.

The amount of vacuum and pressure is read by a spring type centimeter gage. Located in the removable headpiece are the rubber pressure relief valve and plugged opening for the patient's signal line. The plugged opening is also used for administering intravenous solutions. A sliding gage attached to the base of the respirator and parallel to the sliding base of the motor is calibrated from 0 to 30 respirations per minute and is adjustable for retiming. The gage permits a quick determination of the respiratory rate.

The apparatus was referred by the Council to a qualified investigator for clinical use. He reports to the Council that the apparatus gave satisfactory service.

The Council voted to accept the Columbian Respirator for inclusion on its list of accepted devices.

FARIES S-4 SUNLAMP MODELS 2404-2455 ACCEPTABLE

Manufacturer: Faries Manufacturing Company, Decatur, Ill.

The Faries S-4 Sunlamp is designed to produce ultraviolet radiation within the limits of the standards set by the Council for devices using the term "sunlamp." These standards require that the energy of wavelengths shorter than and including 2,800 angstroms shall not exceed 1 per cent of the total energy of wavelengths between 2,804 and 3,132 angstroms. These wavelengths fall in the spectral region of low erythematogenic action and render the sunlamp suitable for unsupervised use by the layman.

The source of ultraviolet energy, the S-4 bulb, is mounted in reflectors on adjustable supports. This S-4 bulb consists basically of a quartz mercury arc about 1½ inches long, enclosed in a special glass bulb which transmits ultraviolet wavelengths of 2,894, 2,967, 3,024 and 3,132 angstroms (and longer wavelengths) but which cuts off most of the wavelengths shorter than about 2,800 angstroms. The lamp produces the characteristic blue green light of the mercury line spectrum. The total power required is 120 watts; line, from 110 to 120 volts; the lamp operates only on alternating current.

Spectral ultraviolet radiation measurements were made on the S-4 lamp in a laboratory selected by the Council. These

measurements showed that the radiation of wavelengths shorter than 2,800 angstroms is immeasurably small and hence these lamps qualify as sunlamps, so far as spectral quality (wavelength) of radiation is concerned.

In this investigation the lamp was placed close in front of the quartz-fluorite achromatic spectroradiometer, and the spectral intensities were measured with a vacuum thermopile. The relative spectral intensities (galvanometer deflections) corrected for absorption in the spectroradiometer are given in the accompanying table.

Relative Spectral Intensities

Wavelengths (Angstroms)	Relative Energy (Average of Three Lamps) Microwatts per Sq. Cm.
3,132	7.96
3,024	2.59
2,967	1.15
2,894	0.28
2,804	0.09
Total	12.07

The radiation at 2,804 angstroms (and shorter if measurable) is about 0.75 per cent of the total of all wavelengths, including 3,132 angstroms and shorter. Mounted in an aluminum reflector, the radiation at 2,894 angstroms and shorter, relative to the total, would be still lower; hence these lamps comply with the Council's requirements for acceptability of a sunlamp for spectral quality of ultraviolet radiation.

The Council on Physical Therapy voted to accept the Faries S-4 Sunlamp for inclusion on its list of accepted devices.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

AMPULS OF CAMPHOR.—"Ampuls of camphor contain a sterile solution of approximately 20 Gm. of camphor in a sufficient quantity of ampul oil to make 100 cc., unless another concentration of the solution is stated on the label, and yield not less than 93 per cent and not more than 103 per cent of the labeled amount of camphor." *N. F.*

For standards see the National Formulary under Ampullae Camphorae.

Actions and Uses.—Parenterally to sustain the circulation and respiration in collapse.

Dosage.—1 cc. containing about 0.2 Gm. of camphor.

Ampoules Camphor in Oil-Endo 0.2 Gm. (3 grains), 1 cc.: Each cubic centimeter contains camphor 0.2 Gm. (3 grains) in olive oil q. s. Manufactured by Endo Products, Inc., New York.

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IRON AND IRON COMPOUNDS (See New and Non-official Remedies, 1940, p. 307).

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THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JULY 27, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

"SARCOIDOSIS"

Medical literature, particularly during the past four years, reveals a renewed interest in this disease of many eponyms. A research by Francis Hunter¹ into the history of its discovery has established that the first description of a case was given by Jonathan Hutchinson in 1869. Twenty years later (1889) Besnier described a similar case presenting the infiltrating type of cutaneous lesion, to which he gave the name "lupus pernio" (chilblain lupus). In 1899 appeared the important publication of Boeck, in which he described the nodular cutaneous lesions under the name of "multiple benign skin sarcoids" or "lupoids." Heerfordt, a Danish ophthalmologist, described in 1909 the syndrome presenting iritis or iridocyclitis in association with a febrile subacute swelling of the parotids and bilateral facial palsy. The identity of the two was recognized by Pautrier. Kuznitsky and Bittorf reported in 1915 a case of cutaneous sarcoid with evidence of

morbid changes in the lymph nodes, spleen and lungs. Jüngling in 1919 described a roentgenographic entity presenting characteristic appearances in the digits and the metacarpal and the metatarsal bones, to which he gave the term "ostitis tuberculosa multiplex cystoides."

The clinical and the microscopic studies of the Stockholm dermatologist Schaumann,² however, first published in 1914, definitely established the essential identity of these apparently unrelated clinical entities. Schaumann pointed out that the disease may indeed exist in the absence of cutaneous lesions and that it displays a predilection for the lymph nodes, the tonsils, the bone marrow, the spleen, the liver and the lungs; in other words, for the organs of the reticulo-endothelial system. The most frequent and, from the clinical standpoint, the most important localization is in the lungs. Characteristic is the absence or paucity of signs elicited by percussion and auscultation when contrasted with the extensive pulmonary infiltrations revealed by x-ray examination.

The histologic unit, irrespective of localization, is a tubercle-like accumulation of epithelioid cells with occasional central necrosis but never caseation, a few Langhans giant cells and a ring of lymphoid cells. These foci show a pronounced tendency to fibrous and hyaline transformation. The lesion is essentially a granuloma closely resembling that of tuberculosis or of Hodgkin's disease but differing from the former in the absence of caseation and of tubercle bacilli. Because of the predilection for the lymph tissue and its essentially benign course, Schaumann gave it the more or less inclusive term "lymphogranulomatosis benigna." The cutaneous lesions present themselves as chronic painless infiltrations or nodules. There is in most cases a more or less universal, symmetrical enlargement of the lymph nodes. X-ray examination reveals in the great majority of the cases fairly characteristic hilar shadows extending fanwise into the lung fields. Striking also in the symptomatology is the wide dissemination of the lesions and the surprising mildness or absence of the symptoms. The patients may complain of fatigue and of rather considerable loss of weight. The course is usually afebrile, with only slight rises of temperature on the appearance of new lesions.

The cause of the disease has not been determined. A number of investigators, among them Schaumann, consider it an atypical anergic form of tuberculosis. The opponents of this theory, while admitting a close resemblance of lymphogranulomatosis to chronic miliary tuberculosis, point out certain differences, namely the absence of caseation, the failure to demonstrate either in stained sections, in cultures or in animal inoculations, tubercle bacilli³ and negative reactivity to large doses of tuberculin (1 mg. and more). The proponents of

2. Schaumann, J.: Sur le lupus pernio, Mémoire read before the Société française de dermatologie in November 1914; Lymphogranulomatosis Benigna in the Light of Prolonged Clinical Observations and Autopsy Findings, Brit. J. Dermat. 48: 399 (Aug.-Sept.) 1936.

3. Harrell, G. T.: Generalized Sarcoidosis of Boeck, a Clinical Review of Eleven Cases, with Studies of the Blood and the Etiologic Factors, Arch. Int. Med. 65: 1003 (May) 1940.

1. Hunter, F. T.: Hutchinson-Boeck's Disease (Generalized "Sarcoidosis"): Historical Note and Report of a Case with Apparent Cure, Brit. J. Dermat. 21: 346 (Feb. 20) 1936.

the tuberculous nature of the disease, however, regard the last phenomenon as anergy and urge in favor of their hypothesis the close morphologic resemblance, the occasional demonstration of tubercle bacilli, the fact that many of the patients eventually die of frank caseating tuberculosis, and the apparent mutual exclusiveness of sarcoids and tuberculous lesions. Thus, as observed in a number of instances, the sarcoid lesions disappeared with the development of a frank tuberculosis and the previously negative tuberculin test became positive. In some instances the removal of the tuberculous focus was followed by the return of sarcoids and a negative tuberculin reactivity. A number of investigators, among them Kissmeyer,⁴ do not believe in the tuberculous etiology and regard such cases in the light of coincidental existence of two distinct entities. In view of the repeated negative bacteriologic studies, Kissmeyer believes that the disease is due to an unidentified virus.

METABOLISM OF IRON

Studies on the metabolism of iron are complicated by a number of physiologic variables beyond the control of the investigator. Iron exists in many combinations and in many places in the body, some of the most important being red cell hemoglobin, muscle hemoglobin, liver, spleen and marrow tissue. Further complications arise from the fact that in a single tissue the iron may exist in several different forms; in the spleen, for example, as iron in the parenchyma, as iron in the contained blood of the organ and as storage iron. Finally, and not unimportant in contributing difficulties to the problem, is the question of accurate quantitative determination of iron in tissues containing interfering minerals, e. g. salts of calcium and phosphorus. Again, the factors influencing the absorption of iron from the gastrointestinal tract, and the relation of the type of iron in the diet and the gastric acidity to this question, the mode of disposition of absorbed iron, the factors controlling the mobilization of iron by the organism, the iron turnover by various depots, the iron transport in the body and the excretion of iron are all problems of prime importance. They concern the understanding not only of the normal metabolism but also of iron metabolism in disease, notably anemia.

Through the medium of the cyclotron of the Research Laboratory at the University of California, radioactive iron has been made available for studies of iron metabolism. The bombardment of the iron isotope of mass 58 with deuterons generated by the cyclotron results in the formation of radioactive iron which decays with the emission of free electrons or beta rays. This radiation can be detected with a suitable physical apparatus and makes possible, therefore, a quantitative determination of radioactive iron. The time required for a loss of half the intensity of this radiation, the so-called half life period for radioactive iron, is forty-seven days,

and this period is ample for the conduct of metabolic studies. The radioactive iron becomes a "marked" element which may be measured quantitatively in body tissues and fluids.

Investigators at the University of Rochester have been concerned for some years with the problems of hemoglobin formation, among which iron metabolism is of prime importance. With the aid of radioactive iron, these workers have now attacked the problems of the absorption, transport, utilization and excretion of iron both in the normal and in the anemic organism. One publication¹ deals with iron absorption; radioactive iron, in the form of ferric sulfate, was administered orally to normal dogs and to dogs made anemic by bleeding. The anemia was maintained for periods of from several weeks to several months by repeated bleeding and maintenance on a diet poor in iron. In the anemic animals, radioactive iron in amounts up to 9 per cent of the administered quantity was absorbed. The material in the colon and feces, when assayed for radioactive iron, accounted for up to 70 per cent of the administered isotope; the remaining unaccounted for iron can probably be charged to inefficiency of the methods of recovery used in the experiments. In striking contrast to the data obtained with the anemic dogs are the results yielded by normal animals; in the latter, little (less than 1 per cent) of the labeled iron was absorbed into the organism. The experiments establish the apparent ability of the dog to discriminate physiologically with respect to the quantity of iron absorbed from the gastrointestinal tract; when there is a distinct need, iron will pass from the intestinal tract into the blood stream. The magnitude of the body reserves of iron appears to determine the extent of the absorption of this element. Observations also indicate that iron absorption which does occur takes place in the small intestine and that the colon is not concerned with this process. The transport of iron from the intestinal tract to the various sites of utilization seems to be a function of the plasma. Within a few hours after its oral administration to anemic dogs the radioactive iron also can be demonstrated in the red blood cells.

In a second communication² the Rochester investigators have reported the results of a study of the excretion of radioactive iron after its intravenous injection as ferrous gluconate. Excretion of the iron was followed in the urine, bile and feces; an initial output was observed in urine and feces for a period (from three to fifteen days) following the iron injection and the quantity excreted accounted for from 2 to 8 per cent of the injected iron. Although the excretion of iron by way of the kidney subsequently dropped to values approaching zero, the feces contained measurable amounts of radioactive iron during the remainder of the experimental period. Blood destruction produced

1. Hahn, P. F.; Bale, W. F.; Lawrence, E. O., and Whipple, G. H.: Radioactive Iron and Its Metabolism in Anemia, *J. Exper. Med.* **69**: 739 (May) 1939.

4. Kissmeyer, A., and Nielsen, J.: Notes sur l'étiologie des sarcoides de Boeck, *Acta dermat-venereol.* **14**: 283 (Oct.) 1933.

2. Hahn, P. F.; Bale, W. F.; Hettig, R. A.; Kamen, M. D., and Whipple, G. H.: Radioactive Iron and Its Excretion in Urine, Bile and Feces, *J. Exper. Med.* **70**: 443 (Nov.) 1939.

by an acetylphenyl hydrazine injection increased the fecal content of radioactive iron, the loss occurring for the most part through the biliary tract. In animals which did not show blood destruction, little fecal iron (0.01 mg. daily or less) is contributed by the bile. The evidence from these experiments indicates the difficulty with which the dog eliminates iron and supports the previous conclusion that the body controls its iron stores by regulation of absorption of iron rather than by the capacity of the organism to eliminate this element. The excretion of iron which does occur is chiefly by way of the biliary and gastrointestinal tracts in both the anemic dog and the animal with well stored reserves. McCance and Widdowson,³ working with human subjects, concluded that the excretion of iron is so small as to be negligible and that the iron content of the body is usually regulated by control of absorption.

Progress in the problems of iron metabolism have been made possible by means of radioactive iron. It may be concluded on the basis of available data that the absorption of iron is regulated according to the needs of the organism, that absorbed iron is excreted at a low level but at a fairly constant rate in the feces, that this excretion can reach fairly high levels under certain conditions, and that the liver is in some manner concerned with secretion of iron through the biliary tract.

Current Comment

BLOOD GROUPING TESTS IN EVIDENCE

Basing its conclusion primarily on the Report of the Committee on Medicolegal Blood Grouping Tests,¹ adopted by the House of Delegates in 1937, the United States Court of Appeals for the District of Columbia recently accepted as established the scientific value of blood grouping tests to the extent that they disprove paternity.² This case involved the paternity of a baby, born in wedlock. The trial court issued an order requiring the husband, the wife and the child to submit to blood grouping tests and this order was affirmed by the appellate court. Two questions were involved in the case: the right of the trial court to require submission to the tests and the evidential value of the results of the tests. The courts are, as a rule, hesitant to accept observations based on recently developed scientific processes. Perhaps this is as it should be, for often issues are involved that too vitally affect human relations to justify court determinations based on unstable experimental developments. One court has thus expressed the formula that should be applied in determining the acceptance, in evidence, of the results of the application of new scientific processes:

Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult

to define. Somewhere in this twilight zone the evidential force of the principle must be recognized, and while courts will go a long way in admitting expert testimony deduced from a well recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field to which it belongs.³

The admissibility of the results of blood grouping tests has been before the courts on a number of occasions. In some of these cases, where the court has refused to admit the results in evidence, the principal issue has been not the scientific soundness of the tests but the authority of the court to require submission to the tests. As pointed out in the Report of the Committee on Medicolegal Blood Grouping Tests, two states, New York and Wisconsin, had at that time, 1937, passed laws specifically authorizing the courts to require submission to blood grouping tests in cases of disputed paternity and providing for the admissibility in evidence of the results of such tests. In 1939 laws were enacted in Maine, New Jersey and Ohio authorizing the courts, whenever the paternity of a child is a relevant issue in a case, to require the mother, child and reputed father to submit to blood grouping tests. All of the legislation that has been enacted to date provides that evidence of the results of such blood grouping tests will be admissible only when such tests definitely disprove the paternity of the putative father. Granting the right of a court to compel submission to blood grouping tests, either by authority of a special law as exemplified in the states named or under a more embracing statute authorizing the court to compel submission to physical examinations without specifically mentioning blood grouping tests, as was the situation in the recent District of Columbia case, there would seem to be no justification for further hesitancy on the part of the courts to accept as scientifically sound the results of blood grouping tests to the extent that they disprove the possibility of paternity.

SPECIFIC SERUM IN PNEUMONIA CONTROL PROGRAM

In the recent report from the Pittsburgh Department of Public Health¹ on pneumonia treated with a specific serum from Jan. 1, 1939, to Dec. 31, 1939, the mortality was 15.7 per cent as compared to 46 per cent among cases treated by other methods. By eliminating the cases in which pneumonia occurred as a terminal infection, the mortality would have been only 8.5 per cent. A considerable variation was shown, however, in the effectiveness of serum in the different types of pneumococcal infections as well as in different age groups. Other factors likewise modified the results. It is certainly clear that specific serum treatment is effective in most types of pneumococcal pneumonia, though no light is shed by the Pittsburgh report on the comparative value of the newer chemotherapeutic agents or on the question of combined chemical and serum treatment.

3. McCance, R. A., and Widdowson, E. M.: Absorption and Excretion of Iron, *Lancet* 2: 680 (Sept. 18) 1937; The Absorption and Excretion of Iron Following Oral and Intravenous Administration, *J. Physiol.* 94: 148 (Oct.) 1938.

1. Report of the Committee on Medicolegal Blood Grouping Tests, *J. A. M. A.* 108: 2138 (June 19) 1937.

2. *Beach v. Beach*, United States Court of Appeals for the District of Columbia, No. 7559, decided June 28, 1940.

3. *Frye v. United States*, 54 App. D. C. 46, 293 F. 1013, 34 A. L. R. 145.

1. Alexander, I. H.: *Lobar Pneumonia—Pittsburgh, Pennsylvania, 1939*. Department of Public Health, Pittsburgh.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

RETURN YOUR QUESTIONNAIRE!

Within ten days more than 40,000 physicians returned their questionnaires to the headquarters office of the American Medical Association supplying information to be used in the campaign for medical preparedness. An especially augmented staff is already at work checking the replies and preparing punch cards which will be used in making the selection of men for functions in preparedness and functions in any national emergency which may develop.

Every physician should return his questionnaire as soon as possible. Ultimately a punch card will be prepared for each physician in the United States, since it is necessary that every physician be represented in the file. If there is national conscription, physicians will be called as are other citizens of the United States. Great advantage to the physicians, to the Army and Navy Medical Departments, to the United States Public Health Service, and indeed to the country as a whole lies in the development of this material. With the full information once supplied, it will be possible to a considerable extent to fit every physician into work for which he is best suited.

On July 19 the Committee on Medical Preparedness met in the headquarters office of the American Medical Association with representatives of the United States Army and Navy and Public Health Service. Plans were discussed for utilization of medical personnel. There begin to be indications of the many needs which must be filled in the future. Tremendous expansion of industries associated with the manufacture of munitions and military supplies will require numbers of industrial hygienists, physicians and surgeons far beyond the number now available. Examination of many thousands of men associated with the setting up of recruiting centers, training forces and for similar objectives will again require the services not only of physicians capable of conducting routine examinations but of specialists in every medical field. Particularly important are pathologists, clinical pathologists, roentgenologists and experts in the field of cardiology, tuberculosis, and nervous and mental diseases. Finally, it is absolutely necessary to assure continuity of medical service for the civilian population.

Arrangements were made to utilize state and county societies in the extension of this work. If a physician fails to return his questionnaire, it will become necessary to ask his colleagues and his state and county medical society to be of service in determining why the physician failed to cooperate and to insure the eventual return of the information.

At a time when the nation may need the service of every patriotic citizen, the physician owes this obligation to the country and to himself. In a few instances cards and notes have been received from physicians indicating that their sympathies do not lie primarily with the needs of the country. It would be unfortunate

indeed if any considerable number of physicians adopted such a point of view. The more promptly the questionnaires are returned, the greater will be the possibility of eventual action. The more accurately the information is supplied the more rapidly will it be codified. It is not only the medical profession that is on trial in this instance but democracy itself.

THE NATIONAL RESEARCH COUNCIL COMMITTEE ON CHEMOTHERAPY

ORIGIN AND OBJECTS

At the meeting of the Division of Chemistry and Chemical Technology of the National Research Council in Washington, D. C., in April 1939, the opinion was expressed that research work should be stimulated in the field of quinine substitutes and synthetic antimalarials.

While quinine, plasmoquine, atebine and a few other drugs have been useful, there is, in the judgment of the medical profession, great need for something better. The present remedies leave much to be desired from a therapeutic point of view and the price is higher than many can afford to pay. Further, so far as quinine itself is concerned, the world is practically dependent for its supply on Java and the Kina Bureau (its selling agent) and might be cut off from this supply or perhaps compelled to pay exorbitant prices, if Java should be seized by some other nation. The trend is therefore toward synthetics as the direction which holds out the best promise of new and useful antimalarials.

Contrary to popular belief, malaria is still one of humanity's major scourges. India, with a population of some 320,000,000, has a yearly average of from 70 to 80 million sufferers, and President Fossdick of the Rockefeller Foundation, in his recent annual report, has called attention to the threatening situation in South America. In certain tropical countries the incidence of this disease is 100 per cent. Throughout the world it is stated to be the direct cause of approximately a million deaths annually.

Dr. Herbert R. Moody, chairman of the division, was duly empowered to appoint a temporary committee to survey the field of malaria and antimalarials and to report back to the division whether or not it would be advisable to designate a regular standing committee of the division to study, in cooperation with the division of medical sciences, the whole problem of the chemistry and synthesis of antimalarials.

The temporary committee appointed by Dr. Moody, from the division of chemistry and chemical technology, consisted of Dr. Leonard H. Cretcher, assistant director of the Mellon Institute of Industrial Research, Pittsburgh; Dr. Lyndon F. Small, head chemist of the National Institute of Health, U. S. Public Health Service, Washington, D. C., and Marston T. Bogert, emeritus professor of organic chemistry in residence, Columbia University, New York, as chairman.

Later, on the nomination of Dr. Esmond R. Long, chairman of the National Research Council division of medical sciences, the following members for that division were added to the temporary committee: Dr. Lowell T. Coggeshall, International Health Division, Rockefeller Foundation, New York, and Dr. Torald H. Sollmann, dean, Western Reserve University School of Medicine, Cleveland.

The completed committee thus consisted of the following chemical and medical representatives: Lowell T. Coggeshall, Leonard H. Cretcher, Lyndon F. Small, Torald H. Sollmann and Marston T. Bogert, chairman.

As a result of this preliminary survey, the temporary committee reported unanimously that, in its judgment, a regular standing committee of the division of chemistry and chemical technology should be constituted by the National Research

Council, to concern itself not solely with antimalarials, but whose function should be chemistry in the service of medicine and its title Committee on Chemotherapy, with antimalarials as its first assignment.

This broadening of the field to be covered by the committee will not reduce in any way its usefulness in an attack on the malaria problem but will permit it to offer its services in attempts to combat other diseases as well, particularly in those cases in which acute emergencies may arise and our help be welcome. Even in the investigation of antimalarials, other diseases are concerned, for example, the possible use of cinchona alkaloids or their derivatives in the treatment of pneumonia, a problem which has been under investigation by Dr. L. H. Cretcher at the Mellon Institute for a number of years.

At the meeting of the division of chemistry and chemical technology, National Research Council, Nov. 18, 1939, in Washington, D. C., the report of the temporary committee was presented and adopted and the committee was discharged. The division then recommended that the same personnel be appointed as one of its regular standing committees, to be known as its Committee on Chemotherapy. This recommendation of the division was subsequently approved by the National Research Council, and Surgeon General Thomas Parran Jr. of the U. S. Public Health Service gave his prompt consent to the service of Dr. Small on the committee.

The Academy of Tropical Medicine, the American Society of Tropical Medicine and the National Malaria Committee met at Memphis, Tenn., Nov. 21-24, 1939, and unanimously endorsed the program of the committee. The council of the American Academy of Tropical Medicine also expressed its cordial approval of the selection of Dr. L. T. Coggeshall as a member of the committee.

The Symposium on Malaria, May 29-30, 1940, in Atlanta, Ga., called by Surgeon General Parran, for the purpose of a preliminary discussion of the malaria situation in our country; with special emphasis on chemotherapy, was attended by Drs. Coggeshall and Small of the committee.

Section N of the American Association for the Advancement of Science, at its Philadelphia Meeting, Dec. 27, 1940, to Jan. 2, 1941, will hold a symposium on the human malarial, in which members of the committee will participate. The proceedings of this symposium when published will constitute an important review of present knowledge of this disease.

The objects of the committee include:

1. Chemistry in the service of medicine, with special emphasis on the discovery of new and useful synthetic drugs.

2. To bring about a closer cooperation between chemists and pharmacologists interested in the same field. It often happens that an organic chemist synthesizes a new compound of therapeutic possibilities but does not know to whom to turn to have it tested. Similarly, a pharmacologist discovers that a certain chemical exhibits hitherto unsuspected physiologic effects but has no information as to which organic chemists could help him in the preparation of the compound and its more promising derivatives.

3. To help in this direction, the committee should function as a general clearing house for the collection and classification of information as to the chemists, manufacturers, pharmacologists and others in the United States who are now at work in this field, the special lines of investigation they are following, and any other pertinent data. With this information in hand, and that accumulated last summer by the survey of research resources of educational institutions, in men and material, now classified and on file in the offices of the division of chemistry and chemical technology of the National Research Council in Washington, we should be able more intelligently to allocate and evaluate the various research problems to be investigated. In this way we can also be of some assistance in reducing the amount of unintentional duplication and overlapping in research work and suggest important problems for investigation where the need seems clearly indicated.

4. Not to undertake too ambitious a program at the outset, since the field of chemotherapy is a vast one. For the reasons explained in the foregoing pages, malaria has been selected as the first disease to be attacked.

5. To prepare a compact semipopular presentation of the malaria situation throughout the world, particularly in our own land, including a summary of what is going on here and how it is retarded and handicapped by lack of funds, for the purpose of enlisting public appreciation and support.

6. To secure funds from interested individuals, institutions, foundations, firms and others for the support of the work of the committee, the establishment of research fellowships and such other activities as will advance and expedite the achievement of the results sought.

Such a survey is now being conducted to ascertain what investigations are under way or planned for the synthesis of new and useful antimalarials, to compile a list of individuals and firms interested in this field, just what they are doing and (as far as may be possible) in what other directions they are arranging to expand.

Simultaneously, bibliographies, reviews and digests of the literature covering various aspects of the problem are being compiled, but all this work can progress but slowly under existing limitations, and speed is urgently needed; for the medical profession confidently predicts a malaria peak this year or next.

Those individuals, organizations, institutions and manufacturers who are willing to cooperate by supplying the information suggested in the foregoing pages are requested to communicate with the chairman of the committee, whose address until September 20 will be Belgrade Lakes, Maine; after that, Havemeyer Hall, Columbia University, New York.

As this committee has been for some time in touch with many others interested in antimalarials both in this and in other countries and has accumulated considerable information of value, it seems to us wise to publish this statement, in order that confusion and duplication of effort may be avoided and national preparedness advanced more speedily, for we have been informed that other committees and groups have been or are about to be organized to cover much the same field, evidently unaware of the existence of our committee and its activities.

LOWELL T. COGGESHALL.

LEONARD H. CRETCHER.

LYNDON F. SMALL.

TORALD H. SOLLMANN.

MARSTON T. BOGERT, Chairman.

CATASTROPHE UNIT

The organization of a "catastrophe unit" of doctors and nurses on the staff of Queens General Hospital, to function instantaneously in the event of a major disaster in the borough of Queens, similar to the unit on duty at Bellevue Hospital, which has already responded in four disasters of major proportions, was announced recently by Dr. S. S. Goldwater, Commissioner of Hospitals. Another unit, similar to the Bellevue emergency unit, is already on duty at Kings County Hospital, and a fourth unit is in the process of organization at Morrisania Hospital in the Bronx.

The Bellevue emergency unit, which consists of thirteen doctors and fifteen nurses, has been called out four times, the first for an explosion on Twenty-Third Street, the second for service to the battered refugees on the S. S. *Harding*, the third for a theater on One Hundred and Twenty-Fifth Street, the ceiling of which fell down, and the fourth for the recent accident at Grand Central Station. The Kings County unit has not yet been called out.

At Queens the emergency organization will consist of two alternating three squad units with four doctors and four nurses to each squad. Two of the three squads are on active call at all times, while one squad is kept in reserve.

Transportation facilities consist of a specially fitted truck supplemented by the hospital ambulances.

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* Deceased.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Meeting at Centerville.—The northwestern division of the Medical Association of the State of Alabama held a meeting at Centerville, July 25. The speakers were Drs. Jesse P. Chapman, Selma, on "Principles Underlying the Treatment of Anemia"; Harvey B. Searcy, Tuscaloosa, "Conjunctivitis"; Neal L. Andrews, Birmingham, "Symptoms of Anorectal Disease"; James C. Gladney, Jasper, "Diagnosis and Treatment of Coronary Occlusion," and Joseph D. Wilson, Birmingham, "Surgical Management of Goiter."

ARKANSAS

Society News.—A symposium on heart disease was presented at a meeting of the Benton County Medical Society, Pea Ridge, June 13, by Drs. Charles T. Chamberlain, Ralph E. Crigler and William O. Arnold, Fort Smith.—Dr. Silas C. Fulmer, Little Rock, discussed nephritis at a meeting of the Pulaski County Medical Society, Little Rock, June 17.—Dr. P. Leo Hathcock, Fayetteville, addressed the Sebastian County Medical Society, June 11, on "Aleukemic Leukemia."

CALIFORNIA

New Student Health Service Building.—Funds have been appropriated by the regents to construct a \$300,000 student health service building for the Los Angeles campus of the University of California. The plans provide a complete health service for the Los Angeles students exclusive of hospitalization. The regents increased the incidental fee on the Los Angeles campus from \$23 to \$25 for the added service. At present, the limited health service available to a student body of about 8,500 is crowded into cramped quarters and operated by part time employees. On the basis of experience on the Berkeley campus, it is estimated that the health service would require a floor area of about 23,500 square feet.

Society News.—A symposium on urology was presented before the Alameda County Medical Association in Oakland, June 17, by Drs. Arthur E. Dart, Herbert Stewart Kimball, Bean M. Palmer, George G. Reinle, Albert M. Meads and Leon I. Oppenheimer.—Mr. Milton H. Silverberg, Los Angeles, referee, state industrial accident commission, discussed "The Doctor and Industrial Medicine and Surgery" before the San Diego County Medical Society, June 11.

Institute on Psychiatric Education.—The first regional institute on postgraduate psychiatric education of the American Psychiatric Association was held, June 17-29, at Agnew State Hospital, Agnew. These institutes will be held throughout the country, sponsored by the committee on psychiatry in medical education, of which Dr. Franklin G. Ebaugh, Denver, is the chairman. Participating in the institute at Agnew State Hospital were, among others:

Dr. Charles A. Rymer, Denver, assistant director of the Colorado Psychopathic Hospital.

Dr. S. Spafford Ackerly, professor of psychiatry, University of Louisville School of Medicine, Louisville, Ky.

Dr. Wendell S. Muncie, associate professor of psychiatry, Johns Hopkins University School of Medicine, Baltimore.

Dr. Walter L. Treadway, assistant surgeon general, U. S. Public Health Service, now stationed at the University of California Medical School, San Francisco.

Dr. Jacob Kasanin, chief of psychiatric service, Mount Zion Hospital, San Francisco.

FLORIDA

New Health Units.—A public health unit has been created in Dade County with Dr. Turner Elam Cato, Charleston, W. Va., for many years health officer of Kanawha County, in charge. Headquarters for the new unit will be in Miami. New full time departments are also being planned for Hamilton and Nassau counties. This will bring the total number of counties served by accredited local health departments to twenty-one, newspapers reported.

Special Society Elections.—Dr. John W. Alsobrook, Plant City, was named president-elect of the Florida Railway Surgeons Association at its annual meeting in Tampa recently, and Dr. Leland F. Carlton, Tampa, was installed as president. Other

officers include Drs. Zannie Brantley, Grandin, vice president, and Walter C. Page, Cocoa, secretary-treasurer.—Dr. Joseph H. Lucinian, Miami, was elected president of the Florida Radiological Society recently to succeed Dr. Harry B. McEuen, Jacksonville; Dr. John N. Moore, Ocala, vice president, and Dr. Elliott M. Hendricks, Fort Lauderdale, secretary.—Dr. Louie M. Limbaugh, Jacksonville, was elected president of the Florida Internists Society to succeed Dr. William C. Blake, Tampa, at its second annual meeting in Tampa recently. Dr. Kenneth Phillips, Miami, was reelected secretary.

GEORGIA

Society News.—At a meeting of the Emory Medical Alumni Association in Atlanta, June 6, the speakers were Drs. Richard Hugh Wood on "Pitfalls in the Therapeutic Use of Sulfanilamide and Its Derivatives"; Frank K. Boland, acute intestinal obstruction, and Clarence Dixon Fowler, infantile diarrheas.—Dr. Daniel C. Elkin, Atlanta, read a paper on "Aneurysm of the Abdominal Aorta" before the Fulton County Medical Society, Atlanta, June 20.

Hardman Cup Awarded.—Dr. William Howard Hailey, president-elect, Fulton County Medical Society, and Dr. Hugh E. Hailey, Atlanta, jointly received the L. G. Hardman Loving Cup at the annual meeting of the Medical Association of Georgia in Savannah recently for their research on "Familial Benign Chronic Pemphigus." Their work also brought them the L. C. Fischer Prize for the most original research presented before the Fulton County Medical Society in 1931. The Hardman Cup was provided by Dr. Lamartine G. Hardman, late ex-governor of Georgia, for the most original research work presented by a member of the Medical Association of Georgia in the field of public health, medicine or surgery.

ILLINOIS

Committee on Archives.—The Illinois State Medical Society has created a permanent committee on archives to collect pictures and all possible data concerning the early physicians in every county of the state. This action is the result of a photographic display at the recent state medical meeting of about 1,500 pioneer physicians of Illinois together with short sketches showing some of the highlights of their practice. The exhibit was under the supervision of Dr. Carl E. Black, Jacksonville, who has been interested in such a collection for more than fifty years.

The Fifty Year Club.—Dr. Andy Hall, Mount Vernon, was made a member of the Fifty Year Club of the Illinois State Medical Society at a special meeting of the Jefferson-Hamilton County Medical Society in Mount Vernon, June 16. Dr. Hall has been a member of the council of the state society for many years and for four years was director of the state department of public health. Since its organization about three years ago, he has been chairman of a council committee sponsoring the Fifty Year Club. About 240 physicians have been admitted to membership in the club.

IOWA

Promotions at the University.—Dr. Erwin G. Gross, who has been acting head of the department of pharmacology at the State University of Iowa College of Medicine since the death of Dr. Oscar H. Plant last October, has been made head of the department. Walter R. Ingram, Ph.D., has been made professor and head of the department of anatomy, neuroanatomy, histology and embryology, succeeding Dr. Ewen M. MacEwen, who has also been dean of the college since 1935. Dr. MacEwen will continue as professor in the department. Dr. Rubin Flocks was promoted from assistant to associate professor of urology, and Dr. Irving H. Borts to assistant professor of hygiene and preventive medicine.

KENTUCKY

Inter-County Meeting.—The Lawrence County Medical Society recently sponsored an inter-county meeting in Louisa, to which physicians from Eastern Kentucky and adjoining counties in Ohio and West Virginia were invited. Among the speakers were Drs. John W. Scott, Lexington, on "Psychoneuroses as Seen by the General Practitioner"; Irvin Abell Jr., Louisville, "Tumors of the Breast"; Elmer L. Henderson, Louisville, "Tetanus," and Arthur T. McCormack, Louisville, secretary, Kentucky State Medical Association, "Medicine Today." Dr. Robert J. Wilkinson, Huntington, W. Va., showed a motion picture on "Surgery of the Female Pelvis."

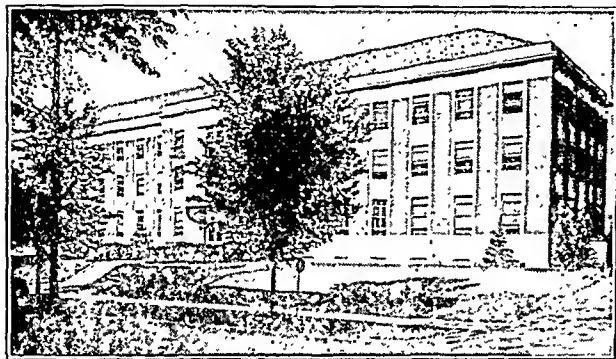
LOUISIANA

Division of Medical Extension at Tulane.—Dr. Hiram W. Kostmayer is now directing the division of medical extension at Tulane University of Louisiana School of Medicine, New Orleans, in combination with his position as director of the department of graduate medical studies.

Society News.—A special report on "Studies on the Bleeding Tendency and Vitamin K Therapy on Newborn Children" was presented before the Orleans Parish Medical Society, New Orleans, June 10, by Dr. Henry Leidenheimer Jr., among other speakers. At a recent joint meeting with the New Orleans Tuberculosis Committee the speakers were Drs. Edward L. Burns on "Pathogenesis and Pathology of Pulmonary Tuberculosis"; Emile F. Nacé, "Early Diagnosis of Tuberculosis from the Standpoint of the Pediatrician," and Morell W. Miller, "Early Diagnosis of Pulmonary Tuberculosis."

MICHIGAN

New University Health Building.—The new \$500,000 health service building at the University of Michigan, Ann Arbor, was recently placed in operation. Accommodations are available for sixty patients. PWA funds were used to construct the building, in which will be available a program of clinical medical service for resident students. Certain attention to faculty members and university employees may be provided, it was said. The use of the hospital connected with the medical school will continue for major surgery, and less frequent highly specialized services. Recent average daily outpatient



New university health building.

visits amounted to 570 and annual regular session bed patient admissions have been 217 per thousand students enrolled. Operating costs of the health service total about \$15 annually for each student, and these are defrayed from the regular tuition fees. Dr. Warren E. Forsythe is director of the health service.

MISSOURI

Officers of Clinical Society.—Dr. Cabray Wortley was recently elected president of the St. Joseph Clinical Society, succeeding Dr. Charles Greenberg. Other officers include Drs. Francis X. Hartigan and Leon Paul Forgrave, vice presidents; Harold E. Petersen, secretary.

Personal.—Edward Adelbert Doisy, Ph.D., professor and director of the department of biochemistry, St. Louis University School of Medicine, received the honorary degree of doctor of science from Washington University, St. Louis.—Dr. Arthur R. McComas, Surgeon, was the guest of honor at a picnic near Columbia, recently, given by the Boone County Medical Society to celebrate his completion of fifty years in the practice of medicine.—Dr. Nathan K. Pope, assistant superintendent of the Missouri State School, Marshall, has been appointed superintendent of the criminal insane division of the Fulton State Hospital, Fulton, succeeding Dr. Thomas R. Frazer, who resigned several months ago.

NEBRASKA

State Medical Election.—Dr. William P. Wherry, Omaha, was named president-elect of the Nebraska State Medical Association at the recent annual meeting in Omaha and Dr. Clayton F. Andrews, Lincoln, was named president-elect. Drs. Albert A. Ashby, Fairmont, and Albert L. Cooper, Scottsbluff, were elected vice presidents. Dr. Roy B. Adams, Lincoln, is secretary. Next year's meeting will be in Lincoln, May 5-8.

NEW YORK

Personal.—The Schenectady County Medical Society honored Drs. Henry G. Hughes, Henry A. Kurth and Morris S. Lord at a meeting, June 6, on their completion of fifty years of practice. Dr. Frank Vander Bogert, program chairman for thirty years, was presented with a walking stick.—Dr. Albert D. Kaiser, Rochester, has been appointed by Governor Lehman to be a member of the temporary legislative commission to formulate a long range health program, succeeding the late Dr. Thomas P. Farmer, Syracuse.

New York City

Gifts to St. Luke's Hospital.—Announcement is made of the recent donation to St. Luke's Hospital of the following amounts: \$10,000 from an anonymous friend for an endowment fund for special nursing; \$2,000 from various friends to remodel the orthopedic ward; \$2,000 from an anonymous donor for the ear, nose and throat department; \$7,500 each from the estates of Andrew Purdy and Louise Baier to endow ward beds; \$9,000 from the Henrietta T. Jones estate for care of sick nurses; \$6,614.60 for general purposes from churches and friends, and various smaller amounts.

Appointments for Tuberculosis Hospital.—Senior staff members for the city's new tuberculosis unit, the Triboro Hospital, nearing completion in Queens, were announced by Dr. Sigismund S. Goldwater after selection by an advisory committee. Drs. Richard H. Bennett and H. McLeod Riggins will be directors of medicine; Henry W. Louria and Daniel A. Mulvihill, directors of surgery; Abraham Braunstein, Long Island City, visiting physician; Cranston W. Holman and Herbert C. Maier, visiting surgeons. The medical board will now be organized and will nominate additional staff members of all ranks to complete the visiting staff of about eighty members. It is expected that the hospital will be in operation by Jan. 1, 1941.

Dr. Sherman Given Borden Award.—The Borden Award for research in nutrition was awarded to Henry C. Sherman, Ph.D., Mitchell professor of chemistry, Columbia University, at the meeting of the American Home Economics Association in Cleveland, June 23-28. The award is a medal and \$1,000. Dr. Sherman has been on the Columbia faculty since 1897 and has conducted research on enzymes, vitamins and the mineral elements in nutrition. He has served as president of the Society of Biological Chemists and has been honored with the Nichols Medal of the American Chemical Society and with the medal of the American Institute of Chemists. The Borden Award has previously been given to Amy L. Daniels, Ph.D., University of Iowa, Iowa City; Lydia J. Roberts, Ph.D., University of Chicago, and Icie Macy-Hoobler, Ph.D., Detroit.

OHIO

Society News.—Dr. Richard Hotz, Toledo, discussed "Differential Diagnosis of Biliary Tract Lesions" before the Academy of Medicine of Toledo and Lucas County, June 7.—Dr. Richard H. Freyberg, Ann Arbor, Mich., addressed the Mahoning County Medical Society, Youngstown, June 18, presenting "Appraisal of Some Adjuncts in the Treatment of Chronic Arthritis."

Public Health Association.—Dr. Charles A. Doan, Columbus, was reelected president of the Ohio Public Health Association at the annual meeting in Cleveland, June 5, during the annual session of the National Tuberculosis Association. Dr. Henry Kennon Dunham, Cincinnati, and Floyd A. Rowe, Cleveland, were elected vice presidents, and James E. Hagerty, Ph.D., Columbus, secretary. Dr. Herbert R. Edwards, New York, was the guest speaker on "Revitalizing the Tuberculosis Control Problem."

Physicians Honored.—Dr. George C. Jameson, Oberlin, was honored at the recent commencement of Oberlin College on the fiftieth anniversary of his graduation from the college. He was guest of honor at a dinner in recognition of his forty-six years on the faculty committee of athletics and was honorary marshal at the commencement.—Dr. John A. Riebel, Columbus, received the honorary degree of doctor of laws from Capital University, Columbus, at the June commencement.—Dr. Philip Zenner, Cincinnati, a physician for sixty-five years, was the honor guest of the Alumni Association of the University of Cincinnati College of Medicine at its annual dinner, June 6. He was formerly professor of neurology and psychiatry at the medical college and is now professor of neurology emeritus.

PENNSYLVANIA

District Meeting.—A program on diabetes featured a meeting of the Eighth Council District of the Medical Society of the State of Pennsylvania at Warren, June 5. The speakers were Drs. Belford C. Blaine, Pottsville; George Booth, Pittsburgh; Frank A. Evans, Pittsburgh, and Edward W. Alton Ochsner, New Orleans. Drs. Charles H. Henninger, Pittsburgh, president of the state society; Chauncey L. Palmer, Pittsburgh, chairman of the committee on public health legislation, and Walter F. Donaldson, Pittsburgh, secretary, also delivered addresses. Testimonial certificates for fifty years or more of practice were presented to Drs. Myron A. Bailey, Jamestown; Michael V. Ball, Warren; Otis S. Brown, Warren; Burg Chadwick, Smethport; Glenn E. Humphrey, Cambridge Springs; Hugh Jameson, Titusville; Andrew J. Mitchell, Sharon; Hiram B. Russell, Sheffield, and Monroe T. Smith, Warren.

Philadelphia

Personal.—Dr. John F. Sinclair has resigned as medical director of the Babies' Hospital of Philadelphia, it is reported. —Dr. Charles L. Brown has been appointed visiting physician in the medical wards of the Philadelphia General Hospital to succeed the late Dr. David Riesman. —Dr. Alfred N. Richards, professor of pharmacology, University of Pennsylvania School of Medicine, received the honorary degree of doctor of science at the annual commencement of Harvard University, June 20.

Laboratory for Standardization of Biological Stains Moved to Philadelphia.—The research and control laboratory of the Commission on the Standardization of Biological Stains, formerly located at the Arlington (Va.) Experimental Farm of the Bureau of Agricultural Chemistry and Engineering of the U. S. Department of Agriculture, has been moved to the Philadelphia College of Pharmacy and Science. This laboratory was established in 1920, at the suggestion of the Society of American Bacteriologists and under the auspices of the National Research Council, with a grant from the Chemical Foundation. Its work is to analyze dyestuffs to be employed for biological stains for identification and for diagnostic determinations. It also works toward improvement in existing products and the synthesis of new dyes for specific purposes. The chairman of the commission is Harold J. Conn, Ph.D., New York Agricultural Experiment Station, Geneva, N. Y. The director of the laboratory is Mrs. Anis P. Bradshaw.

RHODE ISLAND

State Medical Meeting and Election.—Dr. Frederick V. Hussey, Providence, was named president-elect of the Rhode Island Medical Society at the annual meeting in Providence in June, and Dr. Lucius C. Kingman, Providence, was installed as president. Dr. Guy W. Wells is secretary. Morning sessions were held at Providence hospitals and afternoon programs at the Rhode Island Medical Library. The speakers were:

- Dr. Robert F. Loch, New York, Adrenal Insufficiency and Its Present-Day Management.
- Dr. Elliott P. Joslin, Boston, Incidence of Diabetes in Rhode Island and Other States.
- Dr. Torr Wagner Harmer, Boston, Observations on Hand Surgery.
- Dr. Charles P. Fitzpatrick, Howard, Some Aspects of Convulsive Disorders.
- Dr. Clifton B. Leach, Providence, Lucetic Heart Disease in Rhode Island.
- Dr. Walter G. Phippen, Salem, Mass., Medical Service and the National Health Program.
- Dr. Robert L. Maynard, Burlington, Vt., Reduction of Fractures of the Acetabulum with Penetration of the Head of the Femur into the Pelvis.

At an evening session Clarence C. Little, Sc.D., Bar Harbor, Maine, managing director of the American Society for the Control of Cancer, made an address on "Progress in Cancer Control."

SOUTH DAKOTA

State Medical Election.—Dr. Bertrand M. Hart, Onida, was chosen president-elect of the South Dakota State Medical Association at its annual meeting in Watertown in May and Dr. Oscar J. Mabec, Mitchell, was inducted into the presidency. Dr. Clarence E. Sherwood, Madison, was reelected secretary for a three year term. The 1941 session will be in Mitchell.

TENNESSEE

Regional Meetings.—Dr. George W. Crile, Cleveland, was the guest speaker at the annual session of the West Tennessee Medical and Surgical Association in Jackson, recently, on "Essential Hypertension." Among other speakers were Drs. Jefferson C. Pennington and Spencer Johnson, Nashville, on "Diagnosis and Management of Prostatic Enlargement"; Con-

ley H. Sanford, Memphis, "The Role of Amcbbiasis in Chronic Digestive Disorders" and Arthur F. Cooper, Memphis, on the work of the National Physicians' Committee for the Extension of Medical Service. Dr. George W. Brasher, Jackson, was elected president.—Speakers at the semiannual meeting of the Middle Tennessee Medical Association in Spring Hill, recently, included Drs. Eugene M. Regen and Cobb Pilcher, Nashville, on "Low Backache with the Sciatic Syndrome"; James C. Kelton, Lascassas, "Chronic Mucous Colitis"; Sam C. Cowan, Nashville, "Puerperal Infection," and William R. Cate, Nashville, "Cardiac Asthma." Dr. Bernard H. Woodard, Spring Hill, was elected president.

TEXAS

Course in Obstetrics and Pediatrics.—Baylor University College of Medicine, Dallas, conducted a postgraduate course in obstetrics for general practitioners, May 20-June 15, in cooperation with the committee on postgraduate medical education of the Texas State Medical Association and the division of maternal and child welfare of the state department of health.

Special Society Elections.—Dr. Wilmer L. Allison, Fort Worth, was elected president of the Texas Neurological Society at its recent annual meeting in Dallas; Drs. William Thomas, Terrell, and Elza M. Perry, Dallas, were elected vice presidents, and Melbourne J. Cooper, San Antonio, secretary.—Dr. Khleber H. Beall, Fort Worth, was chosen president of the Texas State Heart Association at its annual meeting in Dallas, May 13; Dr. Edwin Ghent Graves, Houston, was named vice president, and Dr. Victor E. Schulze, San Angelo, secretary-treasurer.

Veteran Physicians Honored.—The Bexar County Medical Society, San Antonio, gave a banquet recently in honor of ten members who have practiced more than fifty years. Dr. Walter G. Stuck presided and delivered an address complimenting the guests of honor, and Dr. Patrick I. Nixon spoke on "Foundation Builders." The veteran practitioners are Drs. Sigmund S. Burg, Oscar B. Manes, James P. Oldham, G. Graham Watts, Frank S. White, John H. Burleson, David Cerna and Edward F. Hertzberg, all of San Antonio; Robert E. Moss, La Grange, and Adolph Herff, Boerne.

Society News.—The Dallas Southern Clinical Society recently elected the following officers: Drs. Everett C. Fox, president; Howard K. Crutcher, vice president, and Charles H. Warren, secretary. The thirteenth annual spring clinical conference will be held at the Hotel Adolphus, March 17-20, 1941.—Drs. Alfred L. Ridings and Max R. Woodward, Sherman, addressed the Hunt-Rockwall-Rains Counties Medical Society, June 11, in Greenville, on "Pathology of the Cervix" and "Feeding of the Sick Infant" respectively.—At a meeting of the Dallas County Medical Society, Dallas, June 27, the speakers were Drs. Hubert F. Hawkins on "Obscure Heart Disease"; Walter H. Moursund, "Heat Exhaustion of Non-industrial Origin," and Claude D. Winborn, "In Defense of Submucous Resection."

VIRGINIA

Personal.—Dr. John E. K. Flannagan, Marion, was recently appointed superintendent and medical director of the Municipal Tuberculosis Sanatorium at Roanoke.—Dr. Clyde F. Ross, Richmond, has been appointed venereal disease control officer of the city, succeeding Dr. Francis W. Upshur.

Eye and Ear Specialists Meet.—Dr. George G. Hankins, Newport News, was elected president of the Virginia Society of Ophthalmology and Otolaryngology at the recent annual meeting at Old Point Comfort. Dr. Mortimer H. Williams, Roanoke, was made vice president and Dr. Guy R. Fisher, Staunton, secretary. The guest speakers were Drs. Lyman G. Richards, Boston, on "Diagnosis and Treatment of Sinus Disease in Children" and Frank B. Walsh, Baltimore, "Ocular Signs of Thrombosis of the Dural Sinuses."

WISCONSIN

Outbreak of Poliomyelitis.—Six cases of poliomyelitis have recently been reported in Florence County. Health authorities asked that public gatherings be restricted and that children be kept at home.

Dr. Koehler Retires.—Dr. John P. Koehler, health commissioner of Milwaukee since 1925, was to retire July 1, according to the *Wisconsin Medical Journal*. Dr. Koehler graduated from the University of Nebraska and the Chicago Theological Seminary before entering Milwaukee Medical College, an immediate predecessor of Marquette University School of Medicine. He received his medical degree in 1911. After several years of practice he was appointed deputy health officer

of Milwaukee in 1918. During his administration the city has won first place in the national health conservation contest four times and second place three times.

Society News.—Drs. Walter A. Fansler, Minneapolis, and William J. Carson, Milwaukee, addressed the Barron-Washburn-Sawyer-Burnett Counties Medical Society in Rice Lake, recently, on "Diagnosis and Treatment of Anorectal Diseases" and "Surgical Infection of the Kidney" respectively.—Drs. Reuben H. Stiehm and William H. Oatway Jr., Madison, addressed the Rock County Medical Society, Janesville, recently, on "Subclinical Pulmonary Tuberculosis" and "Modern Collapse Therapy of Pulmonary Tuberculosis" respectively. Dr. Adrien H. Verbrugghen, Chicago, was the speaker, June 26, on "Treatment of Spinal Injuries."—Dr. Walter A. Brussock, Milwaukee, addressed the Washington-Ozaukee Counties Medical Society, Hartford, recently, on treatment of heart disease.

PUERTO RICO

District Meeting.—At a meeting of the Mayaguez District Medical Society at Yauco, July 7, the speakers included Drs. Ramón T. Colón, Mayaguez, "Prognostic Value of the Conversion of the Sputum"; Thomas H. D. Griffiths, senior surgeon, U. S. Public Health Service, "Protective Measures Against the Introduction of Yellow Fever"; Gabriel E. Rigau, Yauco, "Molasses and Its Use in Medicine"; Ramón M. Suarez, San Juan, "Treatment of the Asthmatic Status"; Manuel Guzman Rodriguez Jr., Mayaguez, "The Hilar Shadow in the Diagnosis of Infantile Tuberculosis." The motion picture "With These Weapons" was shown with introduction by Dr. Ernesto Quintero, San Juan, and Dr. Armando Antommattei, Yauco, reported "A Bicephalic Case."

GENERAL

Meeting of Insurance Physicians.—Dr. Albert J. Robinson, Hartford, Conn., was elected chairman of the medical section of the American Life Convention at the thirtieth annual meeting of this group in Colorado Springs, June 4-6, and Dr. Benjamin F. Byrd, Nashville, Tenn., was reelected secretary. Among the speakers were Drs. Harry E. Ungerleider, New York, on "Cardiac Arrhythmia" and Albert R. Tormey, Madison, Wis., "Osteomyelitis."

Placement Bureau for Use by Radiologists.—The American Registry of X-Ray Technicians announces the establishment of a placement bureau. The services of the bureau will be limited to physician-radiologists of approved standing and x-ray technicians who have been certified by the registry. It will operate without fees. Applicants for positions will be classified according to their added abilities as nurses, laboratory technicians or other qualifications. Physician-radiologists wishing to register a vacancy for an x-ray technician with the placement bureau may do so by writing to Alfred B. Greene, R.T., executive secretary, American Registry of X-ray Technicians, Oak Terrace, Minn.

Cancer Institute to Publish Journal.—The National Cancer Institute, Bethesda, Md., announces the forthcoming publication of the *Journal of the National Cancer Institute*, to be issued bimonthly. The journal will contain articles by members of the staff of the institute, which is a unit of the National Institute of Health, U. S. Public Health Service. The subscription price will be \$3 a year in the United States. The journal will be distributed free to a limited number of medical schools, to workers in the fields of cancer research, to research institutes interested in cancer, to a limited number of surgeons as well as to certain government depositories and to journals making suitable exchanges.

Poliomyelitis Increased in 1939.—A sharp increase in the number of cases of poliomyelitis was reported in 1939 over the total recorded in 1938, according to figures released by the U. S. Public Health Service. There were 7,272 cases in 1939 as compared with 1,705 cases in 1938. The latter was considered a year of unusually low incidence. In 1939 the distribution of the disease was characterized by a number of localized outbreaks in various sections of the country in addition to a fairly widespread occurrence in the mountain states. The case rate was highest in New Mexico, South Carolina, Arizona and Minnesota, followed by Michigan, Utah and California. The most extensive area included a group of counties in Arizona, Utah, New Mexico, Colorado and northwestern Texas. The second largest area extended across central Minnesota and included a few counties in northeastern South Dakota. Smaller groups of counties in which the incidence was high were located in Michigan, New York, South Carolina, Kentucky, Iowa and south central California. Two adjoining

counties in New Jersey and Philadelphia comprised a very small area in which the incidence of poliomyelitis was moderately high.

Changes in Status of Licensure.—The Massachusetts Board of Registration in Medicine reports the following action taken at a meeting June 6:

Dr. Joseph D. Beauparlant, Fall River, license revoked on account of conviction of abortion.

The state board of health of Missouri recently reported the following actions:

Dr. Charles M. Yaley, St. Louis, license revoked, June 6, for unprofessional and dishonorable conduct.

Dr. James Monroe Brotherton, Kennett, license revoked in April for unprofessional and dishonorable conduct.

The Public Health Council of West Virginia reports the following action:

License of Dr. Paul Foreman Weist, formerly of Charles Town, revoked July 1 on the grounds of conviction of a felony under the Maryland Uniform Narcotic Act while he was under probation to the Public Health Council following a previous conviction under the federal narcotic act.

Assistant Managing Director Appointed for Cancer Society.—Dr. James Samuel Binkley, New York, has been appointed assistant managing director of the American Society for the Control of Cancer, effective June 1. He will divide his time between the society and his work on the staff of Memorial Hospital for the Treatment of Cancer and Allied Diseases. Dr. Binkley is a native of Oklahoma and graduated from Harvard Medical School, Boston, in 1932. He engaged in private practice in Oklahoma City and went to Memorial Hospital in 1936 as assistant resident surgeon. During the past year he has been resident surgeon. He spent February and March giving a series of postgraduate lectures in forty towns and cities in Oklahoma under the auspices of the state medical association, the state department of health and the Women's Field Army of the American Society for the Control of Cancer.

Young Physician Disappears.—Dr. Runyon H. Irvin, Mount Vernon, Ill., disappeared from his home June 2 and has not been heard from since. His mother, Mrs. Grant Irvin, requests that any information concerning him be telephoned



collect to her at Mount Vernon, telephone number 1015, or to Dr. Todd P. Ward, telephone 59, Mount Vernon. She asks also that if he is located he be advised to telephone her if he needs funds. Dr. Irvin had suffered a nervous breakdown during the past year but was thought to be improved. He is 32 years old, 5 feet 11 inches tall, weighs 160 pounds, has a fair complexion, light hair and blue eyes. He was wearing a grayish blue winter suit, a white straw sailor hat and black shoes, size 11.

Special Society Elections.—Dr. Paul P. McCain, Sanatorium, N. C., was elected president of the National Tuberculosis Association at the annual meeting in Cleveland, June 3-6. Drs. James Burns Amberson Jr., New York, and Grover C. Bellinger, Salem, Ore., were elected vice presidents and Dr. Charles J. Hatfield, Philadelphia, was reelected secretary. President Roosevelt and Surgeon General Thomas Parran of the U. S. Public Health Service were made honorary vice presidents.—Dr. Clement J. DeBere, Chicago, was elected president of the American Proctologic Society at the annual meeting in Richmond, Va., June 9-11. Dr. John J. Corbett, Detroit, was elected vice president and Dr. William H. Daniel, Los Angeles, secretary.—Dr. Fraser B. Gurd, Montreal, was elected president of the American Association of Thoracic Surgery at its annual meeting in Cleveland in June. Dr. Edward D. Churchill, Boston, was elected vice president and Dr. Richard H. Meade Jr., Philadelphia, reelected secretary.—Dr. Harold G. Trimble, Oakland, Calif., was named president-elect of the American Trudeau Society at its annual meeting in Cleveland, June 3, and Dr. Lewis J. Moorman.

Oklahoma City, became president. Dr. Victor F. Cullen, State Sanatorium, Md., was elected vice president and Dr. Benjamin L. Brock, Waverly Hills, Ky., secretary.—Dr. James A. Babbitt, Philadelphia, was named president-elect of the American Laryngological, Rhinological and Otolological Society at the annual meeting in New York, June 8, and Dr. John MacKenzie Brown, Los Angeles, became president. Vice presidents elected were Drs. Nelson S. Weinberger, Sayre, Pa.; William G. Kennon, Nashville, Tenn.; Walter H. Theobald, Chicago, and Robert C. Martin, San Francisco. Dr. Carlton S. Nash, Rochester, N. Y., is secretary. The 1941 convention will be in Los Angeles.—Dr. Louis Faugeres Bishop Jr., New York, was elected president of the American Therapeutic Society at the annual meeting in New York in June. Dr. Oscar B. Hunter, Washington, D. C., is secretary.—Dr. Bernard J. Alpers, Philadelphia, was elected president of the American Association of Neuropathologists at the annual meeting in Rye, N. Y., June 6; Dr. Roy R. Grinker, Chicago, was elected vice president, and Dr. Armando Ferraro, New York, secretary.

LATIN AMERICA

Congress on Tuberculosis.—The Fifth Pan American Congress on Tuberculosis will be held under the auspices of the Latin American Union of Tuberculosis Societies in Buenos Aires, October 13-15, and in Cordoba, October 16-17. Official subjects for discussion will be the tuberculosis index of South American countries, heredity and contagion in tuberculosis and the lungs in extrathoracic forms of tuberculosis. Each member nation of the union will have an official speaker on each subject. An attendance fee of 10 pesos, Argentine currency, has been set for members of the congress and a fee of 5 pesos for members of their families, allowing them to participate in official activities but not in the deliberations of the congress. Fees may be sent to and other information may be obtained from the chairman, Dr. Gumersindo Sayago, 9 de Julio, 691, Cordoba, Argentina.

CORRECTION

Dr. Jones.—In THE JOURNAL, June 1, page 2230, in an announcement of the annual meeting of the American Neisserian Society, it was stated that a paper on "Correlating the Micro-pathology and the Clinical Findings in Gonorrhea" would be given by Dr. William Ray Jones, Minneapolis. This should have been Dr. Walter Raymond Jones, Seattle.

Government Services

New Director of Malaria Research Laboratory

Dr. Hiram J. Bush, U. S. Public Health Service, has been named director of the Henry R. Carter Memorial Laboratory for Malarial Research, Savannah. He succeeds Dr. Thomas H. D. Griffiths, who was transferred to Puerto Rico several months ago, as chief quarantine officer. Dr. Charles M. McGill has been acting director of the laboratory since Dr. Griffiths' departure. Dr. Bush graduated at the University of Pittsburgh School of Medicine in 1927.

New District Health Unit in New Orleans

The U. S. Public Health Service has established a permanent health district unit with headquarters in New Orleans, newspapers reported recently. The unit will supervise public health service work in Texas, Louisiana, Florida, Alabama, Georgia, Mississippi and Tennessee. Dr. Charles L. Williams, assistant surgeon general, U. S. Public Health Service, will be in charge of the unit, which was expected to begin operations July 1.

New Marine Hospital at Boston

A new building for the U. S. Marine Hospital, U. S. Public Health Service, Boston, was dedicated June 6, with Paul V. McNutt, Federal Security Administrator, as the principal speaker. Drs. Thomas Parran, Surgeon General, and Sanders L. Christian, chief of the division of marine hospitals and relief, U. S. Public Health Service, were other speakers at the ceremonies. At a luncheon in connection with the exercises, Dr. Roger I. Lee, Boston, was the speaker. The new 360 bed hospital is on Warren Street near Commonwealth Avenue.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 29, 1940.

Bomb Hospital Ships

In reply to a question in the House of Commons, the government stated that since the outbreak of war nine hospital ships have been bombed, shelled or machine gunned—two of them on more than one occasion—despite the vessel's distinctive and unmistakable markings and in contempt of the lives of the wounded and of the doctors and nurses attending to them. The hospital ship *Atlantis* alone was bombed no less than five times in Norwegian waters. The only sinking was that of the hospital carrier *Paris*, June 2, which succumbed to three separate waves by bomber aircraft. The hospital carrier *Brighton* was holed and run aground; the hospital carrier *Maid of Kent* was set on fire. In his speech dealing with the embarkation of the allied troops from Dunkirk, Mr. Churchill stated that the hospital ships which brought off many thousands of British and French wounded, though plainly marked, were a special target for enemy bombs. The *Paris*, which had no wounded on board at the time of the bombing, had to be abandoned after the dropping of twelve bombs. An hour later the aircraft returned and machine-gunned the army medical corps and the nurses who were taking to the boats. A bomb hit the davit of a boat carrying six nurses, throwing them into the sea. They were pulled out with ropes, but one was badly wounded in the arm. It was suggested in Parliament that as the Red Cross is not respected and even seems to attract attack, its use should be discontinued, but a decision on this point has not been made. It has also been suggested that hospital ships should be armed or convoyed.

Americans Give Ambulances

As a gesture in the present emergency, Americans in Britain are to equip and maintain a large ambulance service, which will be known as the American Ambulance, Great Britain. It will number at least 200 well equipped ambulances and mobile first aid units. The drive to raise funds was launched not long ago by well known members of the American colony in London. Funds will be raised entirely from American individuals and social and commercial organizations here and in the United States. A start was given when the American ambassador, Mr. Joseph Kennedy, made in the name of his wife a contribution sufficient to supply and maintain a completely equipped ambulance for one year. Mr. Kennedy's gesture has been followed by the gift of six eight cylinder saloon cars from Packard Cars. Four Chrysler and two eight cylinder Dodge cars have been contributed by Chrysler Motors Ltd.

Departure of Sir Aldo Castellani

On the entry of Italy into the war the large Italian population in this country was interned. But a party of Italians, amounting to 700, consisting of consuls and others, have been shipped to Italy with the Italian ambassador. Among these was Sir Aldo Castellani, the authority on tropical medicine. An Italian by birth, he settled in London, where he attained high position, becoming a fellow of the Royal College of Physicians and director of mycology and lecturer at the London School of Tropical Medicine. He received the decoration of K.C.M.G. from the British government and was editor of the *Journal of Tropical Medicine*. He was the principal medical officer in the Italian expedition against Abyssinia. At one time he held the chair of tropical medicine at the Louisiana State University, New Orleans.

Italy as a Source of Drugs

The entrance of Italy into the war has removed a source of drug supply, particularly of essential oils. Great quantities of Sicilian lemon, orange, bergamot and mandarin oils are shipped from Messina to the world's trading centers, but fortunately these articles are produced on a large scale in other countries. In recent years Italian shippers have met with increasing competition, notably from the California producers of lemon oil and West African producers of orange oil. California is now sending to this country a cold pressed lemon oil (as distinguished from the distilled oil) which compares favorably in taste and aroma with the celebrated Sicilian hand pressed oil and is sold at half the price. French Guinea began to export orange oil in recent years and has made remarkable progress. At one time Italy possessed almost a monopoly of citric acid, but this trade is now of little importance because of the large production of synthetic citric acid. The stoppage of exports from Bari of Italian olive oil is not of great moment, as vegetable oils such as peanut, sesame and cottonseed oil are equally suitable for edible and for medicinal uses. Squill and manna come so much from Italy that there is a shortage, but the latter is not now much used in medicine. Liquorice juice and sulfur come largely from Italy but there are important other sources.

The British Postgraduate Medical School

The dean's annual report of the British Postgraduate Medical School states that the year has been one of steady progress in the development of postgraduate education. The most noteworthy advance was provision of an organized course for the diploma in clinical pathology. This has been available for the last eight years, but up to 1937 only five candidates had satisfied the examiners. This was mainly due to difficulty in obtaining instruction covering the whole field. Applications for the course were received from India and the dominions as well as from home. Only half the applications for admission could be accepted. A testimony to the standing of the school is that the American Board of Internal Medicine has recognized it as one of the foreign medical schools where students may spend the first three years in study.

BUENOS AIRES

(From Our Regular Correspondent)

June 7, 1940.

Number of Physicians in Argentina

According to the report of a special commission, there are 11,244 physicians in Argentina, one for every 1,485 inhabitants. Of these, 5,077 live in Buenos Aires. This leaves some parts of the country scantily provided. In several northern provinces, for example in Santiago del Estero and in San Luis, one physician is found to 5,569 and 5,645 inhabitants, respectively. In the province of Tucumán the proportion is that of one physician to 3,048 inhabitants, but of the 164 physicians 120 reside in the capital of the province (125,000 inhabitants) leaving forty-four physicians for the rest of the province (375,000 inhabitants), which means a ratio of one physician to 8,522 inhabitants. In the city of Buenos Aires the ratio is one physician to 625 inhabitants.

Transporting Patients by Airplane

Dr. Mariano R. Castex, professor of internal medicine in Buenos Aires, with the collaboration of Dr. Capdehourat and Dr. Orosco, investigated the effect of the transportation by air on persons with cardiac and pulmonary diseases. They utilized the data obtained by the scientific mission sent by Argentina to the Bolivian plateaus. Low barometric pressure, they found, provokes a syndrome of hypoxemia and hypocapnia. Gas alkalosis induced by increased excretion of carbon dioxide favors arterial oxygenation by influencing the hydrogen ion concen-

tration toward the alkaline side. These modifications together with the increase of erythrocytes and hemoglobin constitute the chief factors in adjustment to the altitude. Careful analysis of the effect of altitude on the heart, lungs and respiratory apparatus of normal as well as ill persons has led Castex and his associates to the conclusion that of persons with cardiac and circulatory disorders only those with myocardia can be safely transported through the air, under certain conditions. In cases of respiratory disorders only those affected with bronchial or chronic pleural disorders of a nonexudative nature can be safely flown through the air. In general, the investigations showed that the effects on persons who fly at a high altitude are analogous to those on persons who live at high altitudes. The only difference consists in the duration of the effect.

Congress for Social Welfare

The first meeting of the National Congress of Sociology, Social Welfare and Medical Needs of Workers is to meet in Córdoba October 14-19. The section on legislative proposals will deal with the relation between cardiopathies and occupational illnesses, carcinoma as an occupational illness, tuberculosis, agricultural labor, revision of the law governing accidents during work, and occupational diseases. The section on social welfare will deal with social security, the constitution of workers and the employment of those under age. The section on medical needs of workers will discuss cancer prevention, pneumoconiosis, neuroses due to occupational work and whether carcinoma, tuberculosis and cardiopathies are to be regarded as occupational illnesses.

Control of Infectious Diseases

Recently the Argentine society of epidemiology and control of infectious diseases (Sociedad argentina de epidemiología y lucha contra las enfermedades infecciosas) was founded in Buenos Aires. Its purpose is to promote research, develop training courses and establish close contact with similar societies abroad. It will work in cooperation with the José Penna Institute for Infectious Diseases of the medical faculty of Buenos Aires. Professor Carlos Fonso Gandolfo was elected president. The institute has been granted permission to sell patriotic stamps to be released annually May 25, the Uruguayan memorial day, to raise funds for fighting infectious diseases.

Joint Sessions of Pediatric Societies

The tenth session of the pediatric society was held jointly with the Uruguayan pediatric society to commemorate the twenty-fifth anniversary of the latter society. Representatives from the United States, Argentina, Chile, Paraguay and Ecuador participated. The Instituto internacional Americano de protección a la infancia also took part in the celebration. The subjects discussed included electrocardiography in pediatrics and the etiology of infections in children's diarrhea. Technical commissions are to be sent to Bolivia and Paraguay to study the morbidity and mortality in children and to work out a plan for child protection. Extensive investigations are also to be undertaken relating to the nutrition of children and mothers in Latin America.

Obstetric Facilities in Venezuela

Oropeza recently reported that in 1936, on the average, 469 births took place every month in the city of Caracas, 170 in public and private institutions, 150 at home under the care of physicians and the remaining 149 managed by midwives mostly without special training. Since 1936 an obstetric clinic has been constructed in which about 263 deliveries take place every month out of 565 monthly births now reported. Caracas, the capital of the nation, is the only city which possesses a well organized medical organization of a public nature. In the remaining cities of the country almost all children are delivered by untrained

midwives. In spite of these conditions, one of the significant causes of children's mortality, namely tetanus, has been reduced from 2,324 in 1922 to 871 in 1932 and to 225 in 1938. The division for mothers and children of the department of health and social aid, in the bulletin of which Oropeza's article appeared, has issued directions governing obstetric aid, the most important and dangerous infant diseases and proper nutrition. In the state budget for last year 1,200,000 bolivares (about \$240,000) was allocated for child aid. This sum is exclusive of subsidies to other institutions.

Child Welfare

The bureau of maternal and child welfare (*dirección de maternidad y infancia*) has been gathering information for two years in numerous private institutions for preschool children. It was found that a large number of children between the ages of 2 and 6 years showed defects or disease conditions. Dental caries and disorders affecting the nose, throat and ears predominated together with parasitism in certain centers. Extensive measures are being taken to combat these diseases by educating the families involved, especially in the poorer sections, and by following up the development of preschool children who have been examined.

Coming Meetings

The eighth congress of the Pan American Medical Association will meet in 1941 in Buenos Aires under the presidency of Prof. José Arce, professor of surgery. It will be organized in twenty-four sections.

The fifth Pan American Conference of National Directors of Public Health is to meet in 1942 in Rio de Janeiro.

An Argentine branch of the Inter-American Society of Microbiology has been organized in Buenos Aires. The society was founded last year in New York in connection with the third International Congress of Microbiology. Prof. Alfredo Sordelli, director of the bacteriologic institute of the national health department in Buenos Aires, is president. Dr. F. Duran Reynals of Yale University is general secretary of the parent association. Further branches are planned for Uruguay, Peru, Chile and Brazil. The Argentine branch is housed in the bacteriologic institute.

The first National Congress of Pediatrics will be held in Buenos Aires October 7-11. The official subjects are growth and physical development, mental development, rickets and the prevention of tuberculosis and syphilis.

Health Propaganda

The national department of public health in Buenos Aires has announced the functions to be exercised by its division on promotion of health and sanitation. It is to educate the public on disease prevention, accidents, drug addiction, poisoning, physical and mental hygiene, and nutrition. A radio program has been arranged furnishing two broadcasts a week over a government station.

Personals

Prof. Angel H. Roffo in Buenos Aires has been nominated *honoris causa* as associate professor of the Universidad Mayor de San Andrés in La Paz, Bolivia.

Prof. Juan Ramón Beltrán, professor of the history of medicine in Buenos Aires, has been appointed an honorary member of the society for the history of medicine in New York.

Prof. B. A. Houssay, professor of physiology in Buenos Aires, has been appointed a foreign member of the U. S. National Academy of Sciences.

Prof. Ignacio Imaz, on reaching the retiring age, has resigned. Dr. Mario Soto, associate professor of pharmacology and therapy on the medical faculty of Buenos Aires, has been named to succeed him.

Marriages

JARROUD BENONIA SMITH JR., A. Surg. Lieut. (j. g.) U. S. Navy, Alva, Okla., to Miss Louise Evangeline Mack of Charleston, S. C., in June.

SANFORD LAMAR BAILEY, Kosciusko, Miss., to Miss Ruth Elizabeth Williams of Mobile, Ala., in Spartanburg, S. C., June 20.

JOHN GEORGE FEDER, A. Surg. Lieut. (j. g.) U. S. Navy, Pensacola, Fla., to Miss Virginia Heard of Atlanta, Ga., June 25.

JOSIAH CLAYTON CARMICHAEL, Birmingham, Ala., to Miss Ruth Kyle Dale at Nashville, Tenn., June 27.

WALTER DARLINGTON HASTINGS JR. to Miss Frances Goldsmith Black, both of Durham, N. C., in June.

JAMES A. FERGUSON, Grand Rapids, Mich., to Miss Margaret Alice Bevan of Elkhart, Ind., in June.

ERNEST WHITMAN FURGURSON, Plymouth, N. C., to Miss Clara Louise Jones of Red Springs in June.

JAMES T. ROGERS, Fort McPherson, Ga., to Miss Miriam L. McKinney of Greenwood, S. C., in June.

STUART N. MICHAUX, Richmond, Va., to Mrs. Ruth Ann Wolfe Benjamin of New York recently.

HAROLD MILTON SMITH, Savannah, Ga., to Miss Madelyn Elizabeth Meredith of Augusta in June.

HENRY EDWARD PLENCE, Charleston, S. C., to DR. RUTH TALLEY SANDERS of Columbia in June.

DAVID BENJAMIN WILSON, McComb, Miss., to Miss Sara Barry Gillespie at Jackson in June.

JOHN L. CASSIDY, Evansville, Ind., to Miss Mary Ann Hickey of Covington, Ky., May 11.

JOHN BERNARD PLUM, Grand Rapids, Mich., to Miss Suzanne Wells of Nashville, Tenn., in June.

FREDERICK E. KREDEL, Charleston, S. C., to Miss Constance Orme in Nashville, Tenn., June 22.

SCOTT LA RUE TARPLEE, Providence, R. I., to Miss Mimi O'Beirne of Atlanta, Ga., in June.

MYRON A. WALKER, Lafayette, La., to Miss June Grace Blevins of St. Francisville in June.

JOSEPH FREDERICK HASLINGER to Miss Dorothy Jerrine Smith, both of Portland, Ore., May 23.

EUGENE R. BENEDETTO, Alliance, Ohio, to Miss Sylvia Zallanta of Columbus, April 27.

LEONARD MARTIN THOMPSON, Lena, Ill., to Miss Esther M. Grier at Minneapolis, June 20.

VERNON LE ROY BAUER, Andrews, S. C., to Miss Sara Louise Hardy of Hemingway in June.

R. PHILIP RUSK, Cadiz, Ohio, to Miss Marguerite Elizabeth Brodbelt of Columbus, June 8.

WALLIS DICKS CONE, Williston, S. C., to Miss Margaret Dickson of Manning, June 12.

SELWYN H. DRUMMOND, Dayton, Ohio, to Miss Virginia M. Gill of Cincinnati in June.

ROBERT A. EVERHART, Columbus, Ohio, to Miss Gertrude Richardson of Ada, June 14.

THOMAS N. MEADE, Goldendale, Wash., to Miss Roselia C. Turley of Yakima, June 22.

TOBIAS STEIN, Huntington, W. Va., to Miss Martha Landau of Newark, N. J., recently.

EDWARD M. BURNS, Freeport, Ill., to Miss Pauline Elizabeth Hackett of Polo, June 18.

JASPER D. BUSH JR. to Miss Irene Satterfield, both of Birmingham, Ala., June 2.

JOHN PARKS BOOKER to Miss Frances Schumacher, both of Wallhalla, S. C., June 17.

LINO J. ARDUINO, Atlanta, Ga., to Miss Elizabeth J. Stemler of Milwaukee, May 22.

MAX R. LONG, Marion, Ind., to Miss Mary McKittrick of Plainville, May 31.

CLAUDE HEARD FORD to Miss Alice Oden, both of Birmingham, Ala., June 1.

JAMES ROWLAND GAY to Miss Lillian Cabell, both of Richmond, Va., July 2.

JOSEPH V. PIRCHIERI to Miss Hortlaine Burns, both of Cleveland, June 8.

H. ROSWELL WAHL, Kansas City, Mo., to Miss Katherine Bell, June 15.

Deaths

Albert Henry Freiberg ☉ Cincinnati, well known as an orthopedic surgeon and as a leader of organized medicine in the state of Ohio, died, July 14, in the Jewish Hospital following an illness of several weeks. He was 71 years old.

Dr. Freiberg was born in Cincinnati Aug. 17, 1868, and received his degree in medicine from the Medical College of Ohio, Cincinnati, later the medical department of the University of Cincinnati, in 1890. Following his graduation he did post-graduate study in Würzburg, Berlin, Strasbourg and Vienna and took up the practice of medicine in Cincinnati in 1893. From 1902 to 1938 he was professor of orthopedic surgery at the University of Cincinnati College of Medicine and since 1902 devoted his time fully to that specialty, serving as consulting orthopedic surgeon to the Cincinnati General and the Children's Hospital and as director of the orthopedic service of the Jewish Hospital. He was elected president of the American Orthopedic Association in 1910 and was chairman of the Section on Orthopedic Surgery of the American Medical Association, 1917-1918. In 1923 he was elected president of the Academy of Medicine of Cincinnati and in 1929 president of the Ohio State Medical Association. His affiliations in scientific organizations included fellowship in the American College of Surgeons and in the American Academy of Orthopedic Surgery as well as in the other organizations which he served as a leader. He gave freely of his time to many civic affairs, holding among other appointments that of member of the Advisory Committee on Crippled Children for the Children's Bureau of the United States Department of Labor. He was a member of the board of trustees of the Cincinnati Institute of Fine Arts and a member of the board of governors of the Hebrew Union College. On Dec. 6, 1939, the president of the University of Cincinnati and the faculty of the College of Medicine sponsored a dinner in honor of Dr. Freiberg.

In 1915 Dr. Freiberg was awarded an honorary LL.D. degree by Cedarville College. He was recognized as a competent amateur botanist and photographer. He played first violin in a string quartet which had met weekly for more than thirty years. He had contributed more recently of his efforts to the work of the Georgia Warm Springs Foundation and of the National Foundation for Infantile Paralysis. His death was recognized by editorial comment in Cincinnati newspapers, which pointed particularly to his sense of social obligation and to his innumerable contributions of service to the poor.

John Gerald FitzGerald, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1903; professor of hygiene and preventive medicine, dean from 1932 to 1936 and lecturer in bacteriology from 1909 to 1911 at his alma mater; director of the School of Hygiene and of Connaught Laboratories, University of Toronto; associate professor of bacteriology at the University of California, Berkeley, from 1911 to 1913; in 1936 was appointed a member of the Permanent Commission on Biological Standardization of the Health Organization of the League of Nations; member of the American Association of Pathologists and Bacteriologists and the Society of American Bacteriologists; fellow of the American College of Physicians; was a scientific director of the International Health Division of the Rockefeller Foundation; in 1937 was a Chadwick lecturer in London; served during the World War; author of "Practice of Preventive Medicine"; aged 57; died, June 20.

Francis Randall Hagner ☉ Washington, D. C.; Columbian University Medical Department, Washington, 1894; professor of genito-urinary surgery from 1905 to 1939, when he became emeritus professor at his alma mater, now known as the George Washington University School of Medicine; past president of the Medical Society of the District of Columbia, the American Association of Genito-Urinary Surgeons and the Clinical Society of Genito-Urinary Surgeons; member of the Southern Surgical Association and the American Urological Association; fellow of the American College of Surgeons; attending genito-urinary surgeon to the George Washington University and Garfield Memorial hospitals; consulting genito-urinary surgeon to the Children's and Gallinger Memorial hospitals; aged 67; died, July 7.

Elsworth Striker Smith ☉ St. Louis; St. Louis Medical College, 1887; an Affiliate Fellow of the American Medical Association; member of the House of Delegates of the American Medical Association in 1920; clinical professor of medicine at his alma mater, now the Washington University School of Medicine, from 1899 to 1923, professor of clinical medicine in 1924 and later professor of clinical medicine emeritus; past president of the St. Louis Medical Society and the St. Louis

Society of Internal Medicine; fellow of the American College of Physicians; aged 76; physician to St. Luke's Hospital; consulting physician to St. Louis Maternity Hospital and Barnard Free Skin and Cancer Hospital; associate physician to the Barnes Hospital, where he died, June 6, of carcinoma of the stomach.

William Albert Evans ☉ Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; formerly associate professor of roentgenology at the Detroit College of Medicine and Surgery; fellow of the American College of Physicians; member of the executive council and past president of the American Roentgen Ray Society; member of the Radiological Society of North America, Inc., and the American College of Radiology; for many years president of the city board of health; roentgenologist to the United States Marine Hospital and the Harper Hospital; aged 63; died, June 9, of coronary occlusion.

Rexwald Brown ☉ Santa Barbara, Calif.; Northwestern University Medical School, Chicago, 1903; member of the Western Surgical Association; formerly vice president of the Pacific Coast Surgical Association; fellow of the American College of Surgeons; past president of the Southern California Medical Association and the Santa Barbara County Medical Society; chairman of the city board of health from 1930 to 1934; veteran of the Spanish-American and World wars; for many years director of the surgical division and chairman of the executive committee of the Santa Barbara Cottage Hospital; aged 62; died, June 21, of cerebral hemorrhage and hypertension.

Ben Witt Key ☉ New York; University of Pennsylvania School of Medicine, Philadelphia, 1909; member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society and the Association for Research in Ophthalmology, Inc.; fellow of the American College of Surgeons; formerly instructor of ophthalmology at the University and Bellevue Hospital Medical College; surgeon to the New York Eye and Ear Infirmary; consulting ophthalmologist to the French and Lutheran hospitals; aged 56; died, June 5, in the Presbyterian Hospital.

William Morris Butler, Brooklyn; College of Physicians and Surgeons, medical department of Columbia College, New York, 1873; professor of mental diseases at the New York Homeopathic Medical College and Flower Hospital, New York, from 1904 to 1917; member of the state board of medical examiners from 1892 to 1903; formerly neurologist to the Cumberland Street Hospital and consulting alienist to the Middletown (N. Y.) State Homeopathic Hospital; aged 90; died, June 22, of senility.

Reese Williams Patterson ☉ Knoxville, Tenn.; University of Louisville (Ky.) Medical Department, 1911; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served during the World War; consulting otolaryngologist to St. Mary's Memorial and Fort Sanders hospitals; consulting bronchoscopist to the Knoxville General Hospital; member of the board of directors of the Lincoln Memorial University, Harrogate; aged 57; died, June 24.

Ralph Edwin Stevens ☉ Chattahoochee, Fla.; Jefferson Medical College of Philadelphia, 1915; member of the Southern Psychiatric Association and the American Psychiatric Association; served during the World War; formerly health officer of St. Petersburg; assistant surgeon, Veterans Administration Facility, Bay Pines, from 1932 to 1935; chief physician to the Florida State Hospital; aged 49; died, June 6, in Sanford of acute dilatation of the heart.

Raymond Tillotson Smith, Fort Smith, Ark.; Loyola University School of Medicine, Chicago, 1926; fellow of the American College of Surgeons; secretary-treasurer and past president of the Arkansas Hospital Association; attending ophthalmologist and otorhinolaryngologist to Sparks Memorial Hospital; on the staff of St. Edward's Mercy Hospital; aged 46; died, June 2, of injuries received in an automobile accident.

Ferdinand Gisler Angeny, Avon by the Sea, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; served during the World War; formerly bank president; for many years a member of the surgical staff and formerly member of the board of governors of the Royal Pine Hospital, Pinewald, and the Dr. E. C. Hazard Hospital, Long Branch; aged 70; died, June 21, of heart disease.

Samuel James Waterworth ☉ Clearfield, Pa.; College of Physicians and Surgeons, Baltimore, 1893; member of the House of Delegates of the American Medical Association 1917, 1926, 1928; fellow of the American College of Surgeons; past president of the Clearfield County Medical Society; for many years on the staff of the Clearfield Hospital; aged 66; died, June 6, of myocarditis.

Walter Frederick Martin @ Battle Creek, Mich.; American Medical Missionary College, 1903; member of the American Urological Association; fellow of the American College of Surgeons; past president of the Calhoun County Medical Society; urological surgeon to the Battle Creek Sanitarium; aged 65; died, June 11, of lymphosarcoma of the heart.

Harry Addison March, Canton, Ohio; Columbian University Medical Department, Washington, D. C., 1901; served during the World War; formerly county coroner; was known as the "father of professional football," having organized the New York Giants and the Canton Bulldogs; aged 61; died, June 10, of uremia and chronic nephritis.

Harry Hymen Tanzer @ East St. Louis, Ill.; St. Louis University School of Medicine, 1926; assistant in gynecology and obstetrics at his alma mater; on the staffs of Christian Welfare Hospital and St. Mary's Hospital; aged 40; died, June 10, in St. Mary's Hospital, St. Louis, of carcinoma of the intestine.

William Napier Macartney @ Fort Covington, N. Y.; University of the City of New York Medical Department, 1888; past president of the Franklin County Medical Society; for many years county coroner; author of "Fifty Years a Country Doctor"; aged 78; died, June 15, of cerebral hemorrhage.

Paul F. Vasterling, Los Angeles; St. Louis Medical College, 1883; member of the Missouri State Medical Association; fellow of the American College of Surgeons; formerly chief surgeon at the Missouri Railway Hospital, St. Louis; aged 77; died, May 31, of carcinoma of the stomach.

George Benjamin Brown, Dyersburg, Tenn.; Memphis (Tenn.) Hospital Medical College, 1899; member of the Tennessee State Medical Association; served during the World War; aged 65; died, June 23, in the Methodist Hospital, Memphis, of uremia.

Frederick James Bruce, Brooklyn; Long Island College Hospital, Brooklyn, 1887; formerly a surgeon in the police department; aged 74; for many years on the staff of the Good Samaritan Hospital, where he died, June 10, of cerebral hemorrhage.

James Andrew Long, Frederick, Md.; Maryland Medical College, Baltimore, 1903; member of the Medical and Surgical Faculty of Maryland; past president of the Frederick County Medical Society; aged 60; died, June 19, of heart disease.

Cecile Markowitz, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1929; member of the board of the Child Welfare Council of Canada; aged 44; on the staff of the Women's College Hospital, where she died, May 14.

Bert Trippeer @ Dwight, Ill.; University of Louisville (Ky.) Medical Department, 1894; Barnes Medical College, St. Louis, 1895; aged 68; died, June 7, in the Grant Hospital, Chicago, of mesenteric thrombosis.

Frank Dunn Mabry @ Port Arthur, Texas; University of Texas School of Medicine, Galveston, 1911; served during the World War; aged 51; died, June 8, in the Nix Hospital, San Antonio, of cerebral hemorrhage.

Ben Clark Gile, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1897; served during the World War; aged 66; died, May 18, in the Presbyterian Hospital of coronary thrombosis.

Herman Janss, Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1899; aged 64; died, May 11, in St. Vincent's Hospital of cardiac infarction.

Leland Eldorus Phipps @ Youngstown, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; served during the World War; aged 55; died, June 2, of coronary occlusion.

Joseph Goodwillie Walker, Wichita, Kan.; University of Nebraska College of Medicine, Omaha, 1903; member of the Kansas Medical Society; aged 64; died, May 5, of coronary occlusion.

William Neumann, New York; Columbia University College of Physicians and Surgeons, New York, 1903; aged 66; died, May 27, in Rye, N. Y., of arteriosclerosis and thrombosis.

William R. Owens @ Glendale, Calif.; Memphis (Tenn.) Hospital Medical College, 1903; aged 63; died, June 7, in the Dickson Memorial Hospital, Paragould, Ark., of heart disease.

Barton Jones Farr, Glen Allan, Miss.; University of Louisville (Ky.) Medical Department, 1898; served during the World War; aged 67; died, May 1, of pulmonary tuberculosis.

Arthur Gilbert Holbrook, Coldwater, Mich.; Jefferson Medical College of Philadelphia, 1899; member of the Michigan State Medical Society; aged 73; died, June 5, of thrombosis.

Samuel Goodman, Boston; University of the City of New York Medical Department, 1889; member of the Massachusetts Medical Society; aged 75; died, May 28, of arteriosclerosis.

James L. Morton, Shelbyville, Tenn.; University of Tennessee Medical Department, Nashville, 1903; county health officer; aged 60; died, May 31, of cerebral hemorrhage.

Robert Carl Van Buren, Carey, Ohio; Eclectic Medical Institute, Cincinnati, 1901; member of the Ohio State Medical Association; aged 63; died, May 31, of heart disease.

Albert L. Corcoran @ Peoria, Ill.; Northwestern University Medical School, Chicago, 1892; aged 70; died, June 3, in the Methodist Hospital of cerebral hemorrhage.

Hannah Yoseph Jacobs, Yonkers, N. Y.; New York Medical College and Hospital for Women, New York, 1894; aged 70; died, May 12, of chronic myocarditis.

Henry Osborn Carrington, Santa Barbara, Calif.; University of the City of New York Medical Department, 1894; aged 82; died, May 28, of coronary occlusion.

Walter John Leo O'Brien @ Boston; Harvard Medical School, Boston, 1898; aged 66; died, May 1, in the Baker Memorial Hospital of intestinal obstruction.

Eugenie Louise Gagnon, Providence, R. I. (licensed in Rhode Island by years of practice); aged 74; died, June 11, of diabetes mellitis and chronic nephritis.

John Hamilton McCoy, Alliance, Neb.; Rush Medical College, Chicago, 1902; aged 63; died, May 17, in St. Joseph's Hospital of cerebral hemorrhage.

Walter Seip Freeman, Philadelphia; Jefferson Medical College of Philadelphia, 1901; formerly a pharmacist; aged 80; died, May 15, of myocarditis.

Walter Howard Fox, Hartford, Mich.; National Medical University, Chicago, 1902; also a dentist; aged 82; died, June 6, of carcinoma of the prostate.

Ralph Pool Grimm @ Farmington, Ill.; St. Louis College of Physicians and Surgeons, 1909; aged 54; was killed, June 23, in an automobile accident.

Robert Acheson Hawthorne, Braddyville, Iowa; Omaha Medical College, 1901; aged 72; died, May 15, in Clarinda of cerebral hemorrhage.

Monroe Thomas Koons, Mulberry, Ind.; Long Island College Hospital, Brooklyn, 1878; aged 91; died, May 14, of chronic myocarditis.

David S. Rowland, Miami, Fla.; Baltimore Medical College, 1893; aged 71; died, May 17, of coronary occlusion and arteriosclerosis.

Nicholas Lawrey, Brooklyn; Maryland Medical College, Baltimore, 1900; aged 69; died, June 7, of chronic myocarditis and arteriosclerosis.

Hiram Clark Moorman, Somerville, Tenn.; Louisville (Ky.) Medical College, 1903; aged 64; died, May 17, of coronary occlusion.

Erich Eisner, New York; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1911; aged 52; hanged himself, May 7.

M. Willard Bigelow, Payson, Utah; College of Physicians and Surgeons, Baltimore, 1911; aged 64; died, May 21, of angina pectoris.

Andrew J. Shores, Los Angeles; University of Louisville (Ky.) Medical Department, 1888; aged 75; died, May 24, of heart disease.

Casper Franklin Jones, Baltimore; Baltimore Medical College, 1895; aged 76; died, May 27, of carcinoma of the prostate.

William Wallace Cook, Los Angeles; Rush Medical College, Chicago, 1898; aged 67; died, June 2, in an automobile accident.

Robert A. Ware, Chicago; Meharry Medical College, Nashville, Tenn., 1910; aged 56; died, May 16, of a gunshot wound.

Robert William Butler, Orlando, Fla.; Rush Medical College, Chicago, 1876; aged 85; died, June 3, of arteriosclerosis.

Frank Lansing Birney, Denver; Rush Medical College, Chicago, 1883; aged 89; died, June 11, of cardiac decompensation.

Boise S. Bomar, Atlanta, Ga.; Atlanta School of Medicine, 1908; aged 55; died, June 4, of coronary occlusion.

Correspondence

HAY FEVER IN CHICAGO

To the Editor:—Two articles have recently appeared in THE JOURNAL which seem to cast doubt on my ability to diagnose hay fever, without offering an iota of fact for the doubt expressed. In the first article, "Potassium Chloride in Allergic Disorders," by George F. Harsh and Paul B. Donovan (May 11, p. 1859), the expressed doubt of my ability to diagnose hay fever was definitely but not too strongly expressed. I quote: "It should be noted that this work was done in Chicago, and the treatment in all these cases was begun on or after Oct. 21, 1938, so that it is highly improbable that any of these patients were suffering from true pollinosis at the time the study was made." This quotation appearing in a highly regarded scientific journal expresses the improbability of my ability to diagnose hay fever but is not backed by scientific facts. My pride was slightly wounded by this unsubstantiated attack on my diagnostic ability, but world events seemed to outweigh my diagnostic acumen so far that I did not take my pen in hand in my defense.

Much to my surprise, on perusing a more recent copy of THE JOURNAL I came on a more severe attack on my ability to diagnose hay fever. Rubin, Aaronson, Kaplan and Feinberg, in an article entitled "Potassium Salts in the Treatment of Pollinosis" (June 15, p. 2359), have the following to say with regard to my diagnostic ability: "Fortunately, the author [Abt] included the dates on which the treatment was begun in the individual patient. It is interesting to note that in the seasonal cases of asthma and hay fever the earliest date on which this medication was administered was October 20. Since it is well known that pollinosis in Chicago terminates before the end of September, it is readily apparent that the conclusions are based on false premises. Had Abt failed to give any dates, which is the case with most authors, this report might have been considered substantial evidence in favor of potassium chloride."

The learned authors who produced this quotation and who state that my conclusions are based on false premises offer no fact or scientific proof that the patients whom I observed were or were not suffering from hay fever. In fact, they have themselves fallen into a grievous error or misconception, for they state that "pollinosis in Chicago terminates before the end of September." Probably many of their patients wish that this statement were a fact. Certainly most of my hay fever patients and my friends and acquaintances and many of my colleagues' patients, friends and acquaintances wish that this statement were a fact.

By definition, hay fever occurs when sufficient pollen causes the symptoms in a sensitive person; this may happen in the middle of August, the middle of September, the middle of October, the middle of November or the middle of any month when pollen and the sensitive individual meet. It would hardly seem necessary to quote authority for this fact.

French K. Hansel (Allergy of the Nose and Paranasal Sinuses, St. Louis, C. V. Mosby Company, 1936, p. 730), in discussing atmospheric studies in the United States and Canada in relation to pollen, under "North Central States" (in which area studies from Chicago are included), notes that "rag-weeds are by far the most important sources of pollen in Illinois." He further states: "In Chicago and surrounding cities on the lake the direction of the wind is more important than its velocity." A final quotation from Hansel's book should suffice; strangely enough, Dr. Feinberg is given as one of the authors for the authority of the following quotation—evidently he has forgotten some of his earlier writings. On page 691 he says: "According to Feinberg and Durham, unusual weather conditions may change the relative severity of the hay fever season and transform a plant ordinarily considered as harmless into an important cause of hay fever." Nowhere in this com-

plete review by Hansel on pollinosis in the Chicago area is the statement made that pollinosis terminates before the end of September.

I should like to present some facts which will purport to show that there was pollen in the air in Chicago in October 1938. In a report obtained through the kindness of O. C. Durham on the pollens found in Chicago during October 1938, the ragweed counts given in the table were noted by him for the following dates (it should be noted that these counts were made from plates exposed on the roof of the courthouse in Chicago, which is in the loop district, and that in all probability if counts had been made in outlying areas, which are in closer proximity to weeds and grasses, such counts would have been higher). Again quoting from Hansel (p. 690): "In 1926 Koessler and Durham made complete field and atmospheric studies of the hay fever causing pollens in 171 mile-square blocks in Chicago and vicinity, and it was found that 38 per cent of the total area is allowed to run to weeds and wild grasses (40,000 acres)."

Thus, through the courtesy of O. C. Durham, I have established the fact that there was ragweed pollen in the air in Chicago in October 1938 and, since my patients lived in Chicago and were sensitive to these pollens and had the classic symptoms of hay fever, my diagnosis was correct.

Botanists teach us, even in our elementary courses, that plants may grow and pollinate until frosts lay them low. This state-

Report of Pollens Found on Atmospheric Slides,
Chicago, October 1938

	Ragweed
October 3.....	2
4.....	10
5.....	5
6.....	2
7.....	2
10.....	5
11.....	2
12.....	3
14.....	4
16.....	1
17.....	1

ment is a basic fact and needs no proof. Through the courtesy of C. A. Donnel of the United States Department of Agriculture, Weather Bureau, I have obtained the monthly meteorologic summary for Chicago for October and November 1938; the authors of the two articles, to whom I am addressing this communication, may obtain similar copies of this meteorologic summary. In the report from the weather bureau for October 1938 no heavy or killing frosts were reported for October 1938. The lowest minimum temperature for the month was 35 F., on October 23 and 24; there was a light frost on October 25 and no heavy or killing frosts reported for October 1938. The average date for the first killing frost of the autumn in Chicago is given as October 19. The report for November 1938 states that the first killing frost occurred November 8.

My thirteen hay fever patients, with one exception, were all seen before the evening of November 8, and the one exception was seen on November 9. The prevailing wind was from the south and southwest for the first half of November, and the wind from this direction sweeps over the prairies and brings the pollen directly into Chicago. These are the facts.

It is interesting to note that Feinberg and his associates report that they made daily pollen counts, and they state in their conclusion: "Reports of therapeutic results in hay fever should be received with skepticism unless they bear the earmarks of evaluation by methods based on relationship of the symptoms to daily, seasonal and geographic fluctuation of the pollen counts." Fortunately in Chicago, through the courtesy of the Abbott Laboratories, daily pollen counts are made by O. C. Durham and are published in the daily newspapers. These accounts are also kept on file, and it would have been quite as

easy for the authors of these two papers to obtain them as it was for me, even after a lapse of eighteen months.

In my article "Note on Oral Administration of Potassium Chloride in the Treatment of Hay Fever, Nasal Allergy, Asthma and Sinusitis" (*Am. J. M. Sc.* 198:229 [Aug.] 1939) I state: "Potassium chloride should not be given in capsules, tablets or powder, in undiluted form. Sodium chloride intake should be limited during the period of treatment." Harsh and Donovan state: "A 5 grain capsule of potassium chloride was given with each meal and sodium chloride was not restricted. Those who experienced gastrointestinal irritation were asked to sprinkle the powder on their food or dissolve it in a glass of water." They state that, although they did not see the logic in following my method of therapy, they adopted it. I would be so bold as to state, and the reader may judge for himself, that the authors did not restrict sodium chloride as advised by me and used on my patients and they did use potassium chloride as a powder in undiluted form and not as I used the potassium chloride in dilution, and therefore I would conclude that they did not adopt my method of therapy.

Recent reports (Rusk, H. A.; Dean, L. W., Jr., and Rindskopf, Wallace: Results of Potassium Therapy in Nasal Allergy, *Ann. Otol., Rhin. & Laryng.* 49:76 [March] 1940; Kern, R. A.: The Role of Water Balance in the Clinical Manifestations of Allergy, *Am. J. M. Sc.* 199:778 [June] 1940) indicate some degree of success in the treatment of pollinosis with potassium chloride. Rusk obtained 33 per cent relief of some degree in thirty patients suffering with ragweed pollinosis. He further says "These patients were all advised to reduce materially the amount of sodium in their diet." Kern states that "By no means all patients, not even a sizeable minority, were helped by potassium chloride alone. The addition of potassium chloride to other types of therapy distinctly improved results in some cases." He further states that "Increased intake of potassium, or decreased intake of sodium, by tending to increase intracellular fluid and to decrease interstitial fluid and edema, will antagonize allergic reactions."

The only object I had in publishing my note on potassium chloride in the treatment of these conditions was to call attention to its availability and to hope that future reports would prove or disprove its merits. I believe that I have accomplished my purpose, as nearly every recent issue of all the first class medical journals in this country seem to have an article on the use of potassium chloride in pollinosis, either for or against. Most of the articles are fair; the two which I have here taken exception to, in that they challenged my ability to diagnose hay fever, seem to me to have been conceived by their authors on the "improbability" and "false premise" that potassium chloride ought not to give results of a positive therapeutic nature; that they did not wish their patients to benefit by this therapy, and they seem to have tried to prove that they did not.

ARTHUR F. ABT, M.D., Chicago.

DEATHS FOLLOWING MAPHARSEN THERAPY

To the Editor:—In their article "Mapharsen in Treatment of Syphilis in Office Practice" in *THE JOURNAL*, Nov. 25, 1939, Rein and Wise mention that "there is not a single recorded instance of aplastic anemia or death which could be attributed to mapharsen." May I kindly call your attention to the article in the *Indian Medical Gazette* (January 1939, p. 24) by Drs. Rajam and Rao of the Venereal Department, General Hospital, Madras, in which they have recorded two deaths, one due to granulocytopenia and the other due to encephalitis following mapharsen therapy.

P. N. RANGIAH, M.B., B.S., Madras, India.
Honorary Assistant Medical Officer, Venereal
Department, Government General Hospital.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

LUBRICATING OILS AND PULMONARY DISEASE

To the Editor:—What deleterious results may ensue in the lungs or tracheobronchial tree from inhalation of a fine mist of oil droplets thrown off from grinding machines in the process of centerless grinding? The cutting oil used is a sulfurized mineral oil containing no halogens. Can changes similar to those of the lipid pneumonias occur from repeated exposures in an eight hour working shift? Over a period of many years no harmful results are known among a large group of employees. However, the question has arisen owing to the recent complaint of an employee of cough and shortness of breath after an exposure to such an atmosphere in the grinding room.

M.D., Ohio.

ANSWER.—Sulfurized mineral oil in distinction to sulfonated mineral oil is an oil containing uncombined sulfur, usually only to the extent of 2.5 per cent but under special conditions up to 5 per cent. Owing to the heat of friction, traces at least of sulfur dioxide may be formed in some industrial operations. Although slight irritation has been noticed, severe injury has not been recorded. In the case of vegetable oils the content of added sulfur may be as high as 10 per cent, thus paving the way for greater amounts of sulfur dioxide. Low concentrations such as 10 or 20 parts per million of air may provoke coughing. Prolonged exposures to sulfur dioxide have been associated with the production of bronchiectasis. Many thousands of workers daily are exposed to lubricating and cutting oil mists without the development of such pathologic states as to attract attention, with the exception of cutaneous lesions. Oil nuclei reaching the terminal air sacs may interfere with gaseous exchange and thus lead to anoxia. However, the quantity of oil in the particle size that will float in the air is so little that the total entering the lung is trivial. Irritation of the respiratory tract from oil mists may arise if the oil contains impurities or if under the action of such agencies as heat has broken down with formation of decomposition aldehydes or the like. Pulmonary cancer has been attributed to lubricating oils but the evidence is doubtful (Touraine, A., and Bour, H.: *Rev. méd. franç.* 20:285 [April] 1939). Unfortunately, pathologists have not directed enough attention to the problem of oil aspiration in industry, and clinicians have made little study of the problem. Much attention has been paid to dusts, but not so much to oil inhalations. Nevertheless, mineral oil is an irritant in the lungs and certainly does no good, even though the harm usually is not great.

MASSIVE DOSE OF VITAMIN D FOR RICKETS

To the Editor:—Has the massive dose of vitamin D (600,000 international units), given subcutaneously or orally, been proved to prevent or cure rickets? Would you advise preventive treatment of rickets by a single injection of this dose given in the fall months? Is it possible that toxic reactions will develop following the single massive dose of the vitamin D? Are commercial preparations available that will permit such large doses?

M.D., New York.

ANSWER.—Rickets can be cured by giving a single dose of 600,000 international units of vitamin D, administered orally in milk. The administration of the vitamin subcutaneously or intraperitoneally has been performed in rachitic rats and on one or two occasions experimentally in the human infant. Altogether there are recorded in the literature approximately 150 children to whom such massive doses of vitamin D have been administered orally.

Recent reports have shown that moderate and severe rickets have been cured by administering 800 units of vitamin D daily, with signs of healing at the end of the first week of therapy and with complete cure at the end of six weeks; a total dosage of one twentieth the amount of the single massive dose accomplishes the same result a little more slowly.

Toxic symptoms have been reported in adults suffering from arthritis with massive doses of vitamin D. It is claimed that the toxicity is due to by-products rather than to the pure vitamin itself.

The use of these massive doses is still in the early experimental stage. The general adoption of this method should certainly await more carefully controlled and more extensive clinical experience. Certain commercial laboratories have preparations with high vitamin D potency.

It is well recognized that surgical cholecystostomies and cholecystenterostomies nearly always close if the common duct remains patent.

Surgical intervention is indicated in cases of persistent internal biliary fistula, since several serious complications may arise from the continuous regurgitation of intestinal contents into the extrahepatic biliary tree. Operative procedures are designed to relieve the common duct obstruction if possible and then to close the fistulous tract at its intestinal entrance. Judd and Burden recommend cholecystectomy in all feasible cases, since the gallbladder is nearly always severely diseased. However, in cases in which the common duct obstruction cannot be relieved it may be necessary to utilize the gallbladder in establishing a more desirable fistula than the one already present.

EXTENSION DEFORMITY OF LEG IN INFANT

To the Editor:—Recently I attended a young primipara who was delivered of a set of twins. Both were of the female sex, the first weighing 5 pounds (2,268 Gm.) and the second 3 pounds 13 ounces (2,637 Gm.). Her pregnancy was normal and her labor not significantly unusual, lasting five hours in all, the only variation being that I found it necessary to apply low forceps for extraction of the first fetus after the head was on the perineum for two hours. The indication for forceps was secondary inertia, possibly resulting from the obstetric analgesia (scopolamine and pentobarbital sodium were employed). The first of the twins was found to have an abnormality of the right lower extremity but was otherwise normal. This anomaly seemed to be in the knee joint, the leg lying hyperextended on the thigh so that the anterior surface of the leg would lie against the anterior surface of the thigh. There was also some angulation tending to displace the leg medially so that the toes would point toward and approximate the opposite grain. As far as I can tell there is no bony anomaly and no dislocation of the joint—that is, there is no anatomic variation from the normal when the affected extremity is lined up and compared with the opposite one. Fluorascopy shows no abnormalities in the bony anatomy and the two extremities appear essentially alike. The leg can be straightened out and flexed, although passive flexion is somewhat restricted as compared to the other side. It is my impression that this congenital defect is the result of malposition in utero, probably the result of pressure from the other fetus, and that the deformity now seen is due to stretching of the posterior capsule and ligaments of the knee joint with some adaptive shortening of the soft structures anteriorly. Incidentally, these are not identical twins, for separate sacs and placentas were present. Two days ago I applied a cast correcting the deformity to that of the normal position, permitting slight flexion (about 15 degrees at the knee joint); also the foot was put up in slight calcaneovalgus position to overcorrect for a slight equinovarus tendency. By this I hope to prevent persistence and exaggeration of the present deformity and possibly to obtain shortening of the posterior capsule and ligaments with resultant restriction of the abnormal mobility. I should greatly appreciate any further suggestions as to treatment, particularly as to whether or not the child should be referred to a specialist without further delay.

J. M. Spatz, M.D., Glasgow, Mont.

ANSWER.—The clinical description of this case has been excellently given. The theory that deformities noted at birth may be the result of malposition in utero has largely been abandoned in the light of more recent and more complete knowledge of embryology. Although the average fetus changes its position often and moves both arms and legs frequently during the later weeks of pregnancy, the complication of the twin may have resulted in the malposition referred to. Against this hypothesis, however, is the fact that the leg could be readily brought down into anatomic position. Had the leg been hyperextended against the thigh for any length of time, it would be reasonable to expect that the anterior soft tissue structures, including the quadriceps muscle and tendons, would have become shortened.

In all probability the leg was injured at the time of delivery. Hyperextension of the leg at the knee during the progress of the labor or at delivery itself may well have dislocated the distal femoral epiphysis, making it readily possible to place the anterior surface of the lower leg in contact with the anterior surface of the thigh. In a small newborn infant, such an injury at the epiphysis may show poorly or not at all in the roentgenogram. Whether or not this deformity had persisted for some time prior to termination of the pregnancy could be best determined by knowing just how difficult it was to straighten the leg to a normal position and subsequently to flex it.

The treatment which has been used is quite correct. The cast may be bivalved after three weeks and gentle massage, passive and active motion in flexion begun while still protecting the leg against complete extension or hyperextension.

Roentgenograms should be made at monthly intervals until the child is at least 6 months of age in order to watch for the development of the centers of ossification in the epiphyses and to determine any evidence of periosteal new bone formation, which would probably appear after two or three weeks, if the deformity was on a traumatic basis.

If a specialist is available it would be advisable to obtain an opinion. It is doubtful, however, if any fault could be found with the manner in which the infant has been cared for.

LIGATION OF FEMORAL VEIN

To the Editor:—What will be the immediate and remote effects of tying off the femoral vein accidentally or purposely to prevent bleeding from a tear at the junction of the femoral and long saphenous veins, during a ligation of the long saphenous vein? M.D., Massachusetts.

ANSWER.—Ligation of the femoral vein proximal to the saphenofemoral junction unquestionably causes temporary edema and cyanosis. The effects of such sudden venous occlusion can be overcome to a great extent by an immediate block of the lumbar sympathetic chain with procaine hydrochloride; this is because a reflex vasoconstriction accompanying the venous obstruction has much to do with production of cyanosis and edema. The extent of the residual edema will depend on the extent of the ascending and descending venous thrombosis which may follow the tying of the femoral vein. This vein has been repeatedly tied below the profunda because of multiple embolizations; reports are also available of the tying of the vena cava which is compatible with well functioning extremities as long as it occurs distal to the renal vein. A collateral venous network is apt to develop in the gluteal, pudendal and suprapubic regions and obviously should not be obliterated.

For all these reasons a lateral suture of the vein should be attempted if feasible and if suitable suture material is on hand.

SKIN FUNGI AND HYDROGEN ION CONCENTRATION

To the Editor:—Would you kindly give me some references concerning the pH of the skin in fungous infection? M.D., New Jersey.

ANSWER.—The following references concern themselves with fungi and hydrogen ion concentration:

Peck, S. M., and Rosenfeld, Herbert: Effects of Hydrogen Ion Concentration, Fatty Acids and Vitamin C on Growth of Fungi *J. Invest. Dermat.* 1: 237 (Aug.) 1938.

Kadisch, E.: Ueber die Bedeutung der Nährbodenalkalität in der Mykologie, *Dermat. Ztschr.* 55: 384 (April) 1929.

Huszek, H.: Ueber den Einfluss des "Wassers" der Zusatzsubstanzen und des pH Auf die Entwicklung der Pilzkulturen, *Zentralbl. f. Bakt.* (pt. 1) 136: 120 (Feb. 13) 1936.

Vamos, L.: Pilze und Wasserstoffionenkonzentration, *Dermat. Ztschr.* 63: 345 (April) 1932.

Talce, R. V.: Le facteur pH en mycologie, *Ann. de parasitol.* 8: 182 (March 1) 1930.

Cerutti, Pietro: Concentrazione idrogenionica e sviluppo degli ifamietti patogeni, *Patologica* 25: 32 (Jan. 15) 1933.

von Mallinckrodt-Haupt, A. S.: Der Wert der pH-Messung bei Pilzkulturen, *Zentralbl. f. Bakt.* (pt. 1) 125: 368 (Aug. 27) 1932.

ALLERGIC HYPOSENSITIZATION

To the Editor:—What percentage of patients allergic to various proteins are benefited by specific desensitization treatment? As a rule how long does a course of desensitization treatment (protein antigens) give relief in those who are completely relieved? D. R. Martin, M.D., Newton, Ill.

ANSWER.—A full treatise on the subject of allergy would be required to answer this question completely. No attempt at hyposensitization should be made if the allergenic substance is avoidable. This is both better and more practical than attempts at hyposensitization. If symptoms are due to substances which cannot be removed from the patient's environment, as pollens, molds and house dust, injection therapy is indicated. The number of injections required for each of these is too variable for practical advice to be given. A few coseasonal injections may be enough in some cases. In other cases from twenty to forty injections may be required to establish a preseasonal dose adequate for relief. The rule is established by the patient and not by the condition. As to the proportion of this group that may be helped, published statistics vary from 70 to 90 per cent of treated patients. It is difficult to establish permanent immunity to any allergic condition. Years of treatment are usually required for the small percentage who are permanently relieved.

The other environmental substances, such as feathers, horse dander, wool and cottonseed, are usually avoidable so that with proper cooperation on the part of the patient treatment by injection is seldom necessary. Hyposensitization is not as satisfactory as with pollens and molds. There are patients who, because of occupational requirements or because of a complicated environment, require injections of such substances as horse dander, cottonseed (dangerous) or feathers, in addition to their complete removal, at least from the bedroom. Such treatment requires extensive experience on the part of the physician. In its absence, the patient is usually better off without treatment.

The injection of food allergens is mentioned only to be condemned. This procedure is seldom necessary, usually ineffective and always dangerous.

PARADOXICAL BREATHING AND RIB RETRACTION IN INFANT

To the Editor:—A child aged 14 months has breathing which has been peculiar since the child was 2 or 3 weeks old. There was some pus in the urine for a while, which cleared up. There has been somewhat of a problem with feeding, which is apparently being satisfactorily adjusted and the child has for some time shown a slow but progressive gain in weight. The child's nervous system appears normal. Breath sounds seem clear on both sides. The heart seems normal. The child has lately developed paradoxical breathing of the anterior inferior half of the chest wall, embodying the lower two thirds of the body of the sternum, xiphoid process and the anterior ends of the lower ribs, drawing in markedly with each inspiration. A diagnosis of fibrosis of the right lung following the use of mild protein silver drops in the nose has been given in this case. I am more inclined to the opinion that there is a congenital disturbance here. I should like to know what possible differential diagnoses should be considered, particularly in relation to this unusual movement of the chest wall.

Philip T. Holland, M.D., Bloomington, Ind.

ANSWER.—The patient presents a picture suggesting an obstruction to the free entrance of air into the lungs with each inspiration. In infants and young children the chondral portion of the ribs is proportionately larger and softer than in older children and adults. Consequently when any narrowing of the airway occurs and the normal negative pressure which is produced by depression of the diaphragm and expansion of the thorax is not being equalized by the ingress of inspired air, a partial vacuum results with the occurrence of certain phenomena in the thorax. The extent of these so-called retractive phenomena depend on the age of the individual and the elasticity of the tissues of the chest and the type of respiration which is normal for that age. The infant's respiration is chiefly abdominal. Abdominal respiration occurs almost exclusively in young infants and gradually changes to the thoracic-abdominal type toward the end of the second year. This change occurs a little earlier in boys. The reason the disturbance in this case apparently has become more marked is that the child has become older and the upper part of the thorax is beginning to expand with inspiration, thereby increasing the negative intrapulmonic pressure with each inspiration.

In view of the mechanics of the respiratory movements, the description presented indicates the presence of some hindrance to inspiration which has apparently been present since birth. Some congenital anomaly of the larynx or trachea such as stenosis of either larynx or trachea, laryngeal webs, relaxation of the aryepiglottic folds or relaxation of the epiglottis. Other conditions which may produce such a sequence of events include mediastinal tumors of a congenital type, such as dermoid cysts or teratoma. In addition, thymus enlargement with tracheal compression should be ruled out. Certainly an x-ray examination of the chest in both the anteroposterior and lateral planes would be of some value in this case and a direct laryngoscopy or bronchoscopy might contribute some pertinent data.

REACTIONS TO SACRAL ANESTHESIA AND PERNICIOUS ANEMIA

To the Editor:—Would you please give me some information on the after-effects of sacral anesthesia performed in the case in question for a rectal operation. The patient developed thereafter slight symptoms indicating involvement of the posterior and lateral columns of the cord with some difficulty in walking and numbness of the lower extremities. The only positive neurologic observations were moderate muscle tenderness in both calves, slight unsteadiness in gait, tenderness on thumping over the sacral spine, absent Achilles jerks, positive Babinski sign on the right and an equivocal Babinski sign on the left. The spinal fluid was under pressure of 150 mm. of water. There was no manometric block. The fluid was clear and colorless and it contained 5 lymphocytes per cubic millimeter. The Pandy and Nonne Apelt reactions were negative; the cerebrospinal Kahn reaction was negative. The colloidal gold curve was 0011000000. The mastic solution curve was flat. There were a trace of globulin and 25 mg. of total protein per hundred cubic centimeters of spinal fluid. No free hydrochloric acid has been found in the stomach after one hour gastric analysis, as a result of which the diagnosis of pernicious anemia has been made. Complete examination has revealed nothing else of importance. Are reactions to sacral anesthesia such as this common?

M.D., Michigan.

ANSWER.—From the experimental and clinical points of view it has been repeatedly demonstrated that spinal anesthesia may be followed by neurologic disorders. These include mild meningeal reactions (leptomeningitis), spinal root lesions (caudal neuritis), more severe meningeal involvement with adhesions to the cord, and occasionally degenerative lesions of the spinal cord. Any one using spinal anesthesia should always be prepared for some complications or sequels. Whenever any substance (liquid, solid or air) is injected into the spinal subarachnoid space a definite meningeal reaction results. The degree and extent of that reaction depend on the strength and quantity of the injected material. These reactions are common but fortunately clear up in the majority of cases. From the objective evidence submitted in this case one can certainly think

of a subacute combined degeneration of the spinal cord due to pernicious anemia and not to the sacral anesthetic, especially if the blood picture is characteristic. The patient should be kept at absolute rest and should receive large doses of liver extract parenterally as well as nicotinic acid.

BRITTLE FINGER NAILS

To the Editor:—A woman of 53 for the past several years has had trouble with her finger nails in that they crack longitudinally and tend to break off before they have grown out beyond the quick. Otherwise the patient appears in good health. Could you give me some lead as to etiology and therapy?

M.D., Massachusetts.

ANSWER.—Brittleness of the nails (onychorrhexis) is a malformation of the nail plate and may occur as a sequel of disturbed function of the matrix due to such causes as (1) primary disturbances of nutrition and defective innervation of the matrix, as in cases of paralysis; (2) secondary interference with the function of the matrix from trauma and malformations of the lateral furrow or inflammations of the underlying connective tissue, such as periostum or bone. The nails may break from slight causes, thus maintaining a partial denudation or continuous irritability of the nail bed. In order to treat the faulty nail formation, an endeavor should be made to remove causes falling in groups 1 and 2, if discoverable, together with use of vitamins A and D and the ingestion of considerable milk to supply calcium. It is well to protect the nail locally by an appropriate pressure bandage made of adhesive tape or wax.

RECURRENT THROMBOSIS AND EMBOLISM

To the Editor:—A woman has been suffering from small painful multiple emboli for the past two years, which have been more frequent recently. Eleven years ago she had thrombophlebitis in both legs following childbirth. For the past nine years she has had large ulcers on the medial surface of both ankles with no evidence of varicosities. During the past six months these have completely healed by the compression type of treatment. I would appreciate any information as to further treatment and prognosis.

M.D., Ohio.

ANSWER.—It is assumed that the correspondent indicates that his patient has had recurrent episodes of pulmonary embolism resulting from venous thrombosis. Because this is an unusual condition, the correctness of the diagnosis should be carefully checked. It is common belief by those who are interested particularly in diseases of the veins that phlebitis is almost never a chronic disease but rather that acute episodes of phlebitis recur. If the case under consideration may be considered an example of recurrent phlebitis with pulmonary embolism, treatment should be directed toward the prevention of recurrence of the phlebitis and venous thrombosis. Unfortunately there is no uniformly successful plan of treatment. However, it is advisable to eradicate foci of infection, to use a vaccine made from organisms cultured from one of the foci, and to have the patient cease smoking if she smokes at the present time. Naturally it is advisable to examine the blood carefully for evidence of dyscrasias which predispose to venous thrombosis.

LOCAL APPLICATION OF SULFANILAMIDE

To the Editor:—I am interested in receiving information on the use of a hot sulfanilamide solution in the treatment of abscess formation.

Frederick L. Scheyer, M.D., Puyallup, Wash.

ANSWER.—F. R. Adams reported at the Greater Philadelphia Dental Meeting, Feb. 1, 1940, good results obtained by the direct injection of a hot sulfanilamide solution into abscesses. There is, however, information available which shows that the local application of crystalline sulfanilamide to infected wounds and open abscesses is a rational therapeutic procedure. Good results have been obtained by the repeated local application of sulfanilamide powder without concurrent oral administration of the drug in infected wounds, superficial ulcers and draining abscesses and sinuses.

HAIR AND PERSPIRATION IN CHINESE

To the Editor:—John Gunther's "Inside Asia," 1939 edition, states on page 285, "Chinese do not perspire; they have no ear wax and very little body hair." I have indeed a great deal of respect for Mr. Gunther but believe the Chinese must perspire it not perceptibly.

R. A. Whitney, M.D., White River Junction, Vt.

ANSWER.—It is not known on what authority Mr. Gunther made his statement, but testimony of educated Chinese residing in this country, as well as observation, fails to confirm his statement as to perspiring. It is true that the Chinese have little body hair as a rule and that ear wax seems to be less abundant, but they are present.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in *THE JOURNAL*, July 20, page 240.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, Sept. 11-13, to be given in medical centers having five or more candidates desiring to take the examination. Part III, Baltimore and New York during October and Boston during November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various centers, Feb. 20. Final date for filing application is December 21. *Oral.* Cleveland, preceding A. M. A. convention. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various centers, Oct. 28. Applications must be on file not later than Sept. 16. *Oral.* Chicago, Dec. 6-7. Applications for Group A must be on file not later than Nov. 1. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* October 21. Applications must be on file not later than September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 18-19. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Cleveland, Oct. 5. *Written.* Various centers, March 8. The only written examination during 1941. Applications must be on file not later than Dec. 1. A special oral and clinical examination will be held on the Pacific Coast during 1941 providing there will be enough candidates to warrant it. Applications for this examination should be on file not later than Sept. 15. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and written.* New Orleans, January 1941. Final date for filing application is November 15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Memphis, Tenn., Nov. 17, preceding the annual meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, December 18-19. Final date for filing application is October 8. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Boston, Sept. 26-29. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Part I. Various centers, October 21. Final date for filing application is September 15. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Oral and Written.* Chicago, February 1941. Applications must be on file not later than Oct. 15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

California Reciprocity Report

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports sixty-six physicians licensed by reciprocity and twelve physicians licensed by endorsement from January 2 through April 26. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Univ. of California	"	"	do, Nebraska
University of Colorado	"	"	Idaho
George Washington	"	"	Colorado
Georgetown University School of Medicine(1933)	"	Penna.
Emory University School of Medicine	"	"	Maryland
Bennett College of Eclectic M.	"	"	Georgia
Chicago College of Med. and S.	"	"	S. Dakota
College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois(1909)	"	S. Dakota
Northwestern University Medical School (1908), (1932), (1936), (1938) Illinois	"	"	Illinois
Rush Medical College(1935)	"	Colorado, (1936)
The School of Medicine of the Division of Biological Sciences	"	"	Minnesota
Univ. of Illi	"	"	Minnesota
Indiana Univ.	"	"	Illinois
State University of Iowa College of Medicine(1930)	"	Indiana
University of Kansas School of Medicine(1936), (1938)	"	Iowa
Johns Hopkins University School of Medicine(1935)	"	Kansas
University of Maryland School of Medicine and College of Physicians and Surgeons(1935, 2)	"	Maryland
University of Minnesota Medical School(1914), (1924), (1925), (1936) Minnesota	"	Utah
St. Louis University School of Medicine(1938)	"	Missouri
Washington University School of Medicine(1929), (1931)	"	Missouri
Craigton Univ. School of Medicine(1933)	"	Iowa, (1936)
Lincoln Medical College of Cotner University(1897)	"	Washington
University of Nebraska College of Medicine(1929)	"	Colorado
Columbia University College of Physicians and Surgeons(1923), (1932), (1933)	"	Nebraska
New York Homeopathic Medical College and Hospital(1924)	"	Kansas
Ohio State University College of Medicine(1921), (1925)	"	Minnesota
			New York
			Ohio

University of Cincinnati College of Medicine(1936)	Ohio
Western Reserve University School of Medicine(1932)	Ohio
(1935) Arizona, (1936) Alabama	"	"
University of Oklahoma School of Medicine(1936)	Oregon
University of Oregon Medical School(1925), (1938)	Oregon
Hahnemann Med. College and Hospital of Philadelphia(1934)	Delaware
University of Pennsylvania School of Medicine(1926)	New York
Woman's Medical College of Pennsylvania(1924)	Ohio
Vanderbilt University School of Medicine(1926), (1936)	Tennessee
University of Manitoba Faculty of Medicine(1925)	Illinois
Western University Faculty of Medicine(1897)	N. Dakota
Deutsche Universität Medizinische Fakultät, Prag(1924)	Massachusetts
Magyar Királyi Erzsébet Tudományegyetem Orvostudományi, Pecs(1926)	Ohio

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists(1929),	(1932)	N. B. M. Ex.
University of California Medical School(1939)	"	U.S.P.H.S.
George Washington University School of Medicine(1920)	"	U.S. Navy
University of Michigan Medical School(1936)	"	U.S.P.H.S.
University of Minnesota Medical School(1915)	"	U.S. Army,
(1931), (1935) N. B. M. Ex.	"	"	"
Cornell University Medical College(1928)	"	N. B. M. Ex.
University and Bellevue Hospital Medical College(1929)	"	N. B. M. Ex.
Duke University School of Medicine(1934)	"	N. B. M. Ex.
Jefferson Medical College of Philadelphia(1924)	"	U. S. Navy

Book Notices

Treatment of Cancer and Allied Diseases. By One Hundred and Forty-Seven International Authors. Edited by George T. Pack, B.Sc., M.D., F.A.C.S., Attending Surgeon, Memorial Hospital, New York, and Edward M. Livingston, B.Sc., M.D., Associate Visiting Surgeon, Bellevue Hospital, New York. In three volumes. Cloth. Price, \$36. Pp. 820; 923-1812; 1815-2598, with 1,500 illustrations. New York & London: Paul B. Hoeber, Inc., 1940.

The object of these large volumes is to assemble in harmonious correlation the widely scattered information about the methods of treating all stages of all kinds of cancer. The editors were impressed particularly with the need of competent and comprehensive presentation of relative values of surgery and irradiation in cancer. It is a remarkable achievement to have brought together and integrated the contributions of 147 leaders in the practical treatment of the cancerous diseases. Of the 147 authors, eleven are European. The vast scope of the volumes is best shown by listing the main topics considered: general principles of treatment, cancer of the mouth and pharynx, larynx, neck, thyroid and parathyroid, breast, chest, esophagus, stomach, intestinal tract (including gallbladder, liver, pancreas, spleen, mesentery, retroperitoneal space), colon, rectum, female genitals, urinary system, male genitals, skin, eye and orbit, nervous system, bone and synovial membranes, lymphoid system, and finally miscellaneous topics (electrosurgery, emergency ligations, rectal anesthesia, fever and lead treatments, care of incurable and terminal cases, nursing in cancer). It is out of the question to comment on single articles and no attention can be given to the way in which the various authors handle their subjects. The articles vary in length from three or four pages to monographic presentations. Many articles have been published elsewhere, notably the overwritten monograph by the editors on the results of the surgical treatment of gastric cancer (Livingston, E. M., and Pack, G. M.: *End Results in the Treatment of Gastric Cancer: An Analytical Study and Statistical Survey of Sixty Years of Surgical Treatment*, New York, Paul B. Hoeber, Inc., 1939; 153 pages with 356 references). The illustrations, all black and white, are uniformly of excellent quality. Many of them are reproductions by the courtesy of publishers of books and periodicals. There are many elaborate and complicated charts and tables, some of which are not easily understood.

Volumes 1 and 2 have separate indexes; at the end of the third volume is the complete subject index for all three volumes. The pages in each volume are given on the backbone. There is no author index. The paper is heavily calendered. Each volume weighs about 6½ pounds. The spacing between the subsections of the text is unusually wide. This is true also of certain tables and especially of prescriptions. The prescriptions for the treatment of incurable cancer on pages 2571-2593 could easily have been printed clearly on half a dozen pages or so. The publishers evidently like wide open spaces. Why overdo? The general typography is of standard excellence, but the section and chapter titles are printed in such large type that one is reminded of newspaper headlines.

Painstaking work by the editors is evident throughout. While each author as a matter of course is responsible for his statements, the editorial supervision has secured a good degree of uniformity of presentation. Uniformity of nomenclature could hardly be expected, however. In the case of some of the contributors there may be a tendency perhaps to rely too absolutely on microscopic structure as a criterion of the radioresistance of certain cancers. All references have been verified. In most cases the references contain the titles of articles in periodicals. The question arises whether such titles are of value enough to justify the labor and space required to print them.

The editors have written valuable introductions to certain sections, e. g. cancer of the breast, esophagus and rectum, and also instructive comments in many places. Special stress has been placed on giving the end results obtained with various forms of treatment.

Enough has been said to make it plain that a contribution of great service has been made to the literature of cancer. An immense storehouse of information and guidance has been provided for all who take direct part in the immediate, practical treatment of the cancerous diseases.

¿Por qué es necesario conocer la historia de un mensaje a García? (Anotaciones para fijar la técnica del Servicio de salubridad de un Terremoto). Por el Dr. Victor Grossi G. (Publicado en la Revista asistencia social). Paper. Pp. 174, with illustrations. Valparaiso, Chile: The Author, 1939.

One shot fired in New England was heard round the world. The message sent by the armed forces of the United States to the Cuban leader of the Spanish-American War of 1898 and immortalized by Hubbard is now being repeated in South America. Army leaders in Russia and Japan have resorted to it as an inspiration to their men. The present author has used it as title and introduction to his description of the work accomplished by the health authorities of Chile in the emergency created by the earthquake that devastated the southern part of the country in January 1939. A number of towns were in ruins and about 30,000 persons had been killed. Sanitation was the most urgent matter, since the deaths exceeded the injured, and the immediate needs were safe water, shelter and protection against disease. One day after the earthquake, physicians and health workers were already on duty furnishing all medical or sanitary relief required by the circumstances. One of the sanitary engineers of the Pan American Sanitary Bureau also arrived and took charge of the water supply problem. In describing in detail the work accomplished, Dr. Grossi, one of the leading participants in the rescue, also emphasizes the need to be prepared for similar disasters in the future and ends with a tribute to the medical profession. In 1939, as previously in 1906, physicians rallied to the call of duty, performed without hesitation the work expected of them, and fulfilled every hope, rising indeed to the needs of the occasion.

The 1939 Year Book of Physical Therapy. Edited by Richard Kovács, M.D., Clinical Professor and Director of Physical Therapy, New York Polyclinic Medical School and Hospital, New York. Cloth. Price, \$2.50. Pp. 472, with 155 illustrations. Chicago: Year Book Publishers Incorporated, 1939.

This is the second yearbook on physical therapy that has been published, and the excellent standard set last year has been maintained in the present edition. The book is divided into two parts. The first part deals with methods of physical therapy and the second with applied physical therapy. The first part is subdivided into sections on general considerations, thermotherapy, fever therapy, electrotherapy, electrosurgery, ultra sound waves, light therapy, hydrotherapy, balneotherapy and climatotherapy, mechanotherapy, occupational therapy and institutional work. The second part is subdivided into sections on general considerations, peripheral vascular diseases, infantile paralysis, pulmonary, abdominal, miscellaneous medical, arthritic and rheumatoid conditions, as well as traumatic and orthopedic, neurologic and mental, pediatric, gynecologic and genito-urinary conditions, including syphilis and gonorrhea. Proctologic, dermatologic and ophthalmologic diseases and also conditions of the ear, nose and throat are considered. The abstracts of material in many foreign languages make this book a noteworthy contribution on contemporary physical medicine. The careful classification of material makes it an excellent reference work

for any one who is desirous of obtaining the latest information concerning the various phases of this important subject. The generous use of illustrations is to be commended and the editor is to be complimented on another extremely interesting edition of this yearbook, which is recommended not only to every physician interested in physical therapy but also to general practitioners and specialists in other fields.

Historia da lepra em S. Paulo. Pelo Flavio Maurano. Volumes I e II. (3.^a Monografia dos Arquivos do Sanatorio Padre Bento). Paper. Pp. 270, with 26 illustrations; 281, with 127 illustrations. S. Paulo: Empresa gráfica da "Revista dos Tribunais," 1939.

The history of leprosy in Brazil may roughly be divided into several chapters. One of the most important is that concerning one of the principal geographic and political divisions of the country: the state of São Paulo. Of the ten chapters in this interesting work, the first two deal with the origin and introduction of leprosy in Brazil and the spread of the disease in Brazilian territory, especially in the state of São Paulo itself, as far back as the eighteenth century and probably long before, with the arrival of Portuguese settlers and especially African slaves. The third is a history of the official action undertaken by various administrations, with the work of the present government being treated in the two final chapters (ix and x). A deserved tribute is here paid to such pioneers as Magalhães, Ribas and Lindenberg, who realized the importance of this question when few indeed even suspected its far reaching scope. Chapter iv describes the lives and history of patients. In chapter v (one of the most interesting parts of Dr. Maurano's book) are discussed scientific concepts and popular beliefs, stress being laid on old confusion as to diagnosis, vogue of certain cures pushed by quacks, and finally the modern scientific period with its many Brazilian contributions. Three chapters (vi, vii and viii) are devoted to civic cooperation in the care of lepers in former times. This book contains information unobtainable elsewhere, which will be received with appreciation by all interested in public health problems of the Americas, among which leprosy stands out. The number of lepers in the state of São Paulo is estimated at more than 15,000. A number of illustrations, including maps, permit a better visualization of many of the points here emphasized. An idea of the magnitude of the task accomplished so far may be gathered from the fact that the number of patients isolated under controlled conditions has increased from less than 500 in 1928 to more than 7,000 in 1938.

The Chemical Composition of Foods. By R. A. McCance and E. M. Widdowson. Medical Research Council, Special Report Series, No. 235. Cloth. Price, \$1.20; 4s. Pp. 150. New York: British Library of Information; London: His Majesty's Stationery Office, 1940.

As a basis for the nutritional and dietetic management of persons with various diseases, it is necessary first of all to have accurate information about the chemical composition of foods. The first comprehensive treatises on the composition of human foods were those of Atwater, published under the auspices of the U. S. Department of Agriculture. Not many investigators have been content to undertake the arduous task of compiling data on foods. It is therefore fitting that Dr. McCance, the senior author, who wished to undertake this project, was granted assistance by the Medical Research Council of Great Britain. The book provides the analytic data which the authors have obtained over a period of many years. There are data on the technic of determinations, notes on the chemical composition of cooked dishes containing several ingredients, with their recipes, and then the tables themselves. The latter, which make up the bulk of the volume, are arranged so as to provide the composition of foods on the basis of 100 Gm. and again in terms of the ounce. The tables provide not only the usual data to be found in most food tables but also data on the available carbohydrate, the anionogen-cationogen value, and data for all the important ash constituents, including sodium, potassium, calcium, magnesium, phosphorus, sulfur, chlorine, iron and copper. Brief supplementary tables provide some data on the so-called available or nonphytin phosphorus in foods and on the percentage of ionogenic iron. There is a suitable index. The foods in the table are divided into cereals and cereal foods (thirty-nine products), dairy products (twenty-two), meat, poultry and game (eighty-two products), fish (eighty-nine products), fruit (seventy-seven products), nuts (ten products), vegetables (sixty-five products),

sugar, preserves and sweetmeats (nineteen products), beverages (sixteen products), beers (six products), condiments (eight products), vegetable fats (two products), cakes and pastries (twenty-eight products), puddings (thirty-six products), meat and fish dishes (thirteen products), egg and cheese dishes (eight products), sauces and soups (ten products). It is apparent that analyses of a great many meats and fish have been made and the data are here made available, frequently for the first time. Among the interesting dishes for which analytic information is made available are bickiepegs, toad-in-the-hole, kedgerree, treacle tart, rock buns, lemon curd tarts and cob nuts. This is the kind of information people interested in foods need to know. While the examples mentioned represent British foods, there are many items of more general use for which data are offered.

Nelson Loose-Leaf Specialties in Medical Practice. Edited by Edgar Van Nuys Allen, M.D., Chief of a Section in the Division of Medicine, The Mayo Clinic, Rochester, Minnesota. With a foreword by Donald C. Balfour, M.D., F.A.C.S., F.R.C.S., Consultant in Surgery, The Mayo Clinic. Volumes I and II. Cloth. Price, \$25 per set. Pp. 441; 443-934, with illustrations. New York & Edinburgh: Thomas Nelson & Sons, 1940.

Supplementing the other well known loose leaf systems in the field of medicine published by the Nelson Company comes a new series to be known as *Specialties in Medical Practice*, edited by Edgar Van Nuys Allen of the Mayo Clinic. The contributors in charge of the various sections are all persons of note in the fields concerned, although in many instances associates and assistants in professorships have been chosen rather than the professors themselves, perhaps because most of these names have already been associated with other volumes. What each of the authors does essentially is to write specifically for general practitioners the information that they should have available regarding various medical specialties. This is done, moreover, in exceedingly brief form, which makes the material much more useful for ready reference than the large volumes now available in most medical fields. One of the best chapters is the section on allergy by F. A. Simon, since this field is so rapidly advancing that one finds it difficult to keep abreast of current literature. Also important is the section on endocrinology. The volume is published in loose leaf form, so that subscribers will no doubt be provided with new pages from time to time as additional information is assembled.

Albert Calmette: Sa vie, son œuvre scientifique. Par P. Noël Bernard et Léopold Nègre. Préface de Pasteur Valléry-Badot. Avant-propos de A. Yersin. Paper. Price, \$1.15. Pp. 271, with portrait. Paris: Masson & Cie, 1939.

The first part traces the course of events in the life of Calmette. He was born in 1863, was promoted "aide-médecin" at the medical school in Brest in 1883 and served as naval medical officer in the Far East, returning to France in 1887. He became interested in the new science of microbiology, subscribed as one of the first to the *Annales de l'Institut de Pasteur*, took part in a course under Roux and met Pasteur himself, through whose influence he was sent in 1890 to Indo-China to establish the first colonial microbiologic laboratory at Saigon. Here he prepared vaccines, worked on fermentations, began his investigations of venoms, which he continued under Roux in Paris after his return to France in 1893, and in 1895 he was appointed director of the Pasteur Institute at Lille, where he remained until 1919, carrying on his practical and investigative work as best he could during the German occupation of Lille from 1914 to Nov. 11, 1918. Here he began the comprehensive work on tuberculosis in all its phases that eventually culminated in the introduction of BCG as an antituberculosis vaccine. In 1919 Calmette was appointed subdirector of the Pasteur Institute in Paris, where in addition to his administrative duties he established new laboratories for the investigation of the prevention of tuberculosis and the production of BCG on a large scale with control of the results of its use. He died in 1933. The many and diverse details of the remarkable career thus outlined in brief fill four interesting, well organized and well documented chapters. The conditions and influences under which Calmette worked are clearly described. His great ability, devotion to service and good will strongly impress the reader. The second part reviews the scientific work of Calmette under the headings of venoms and antivenom serotherapy, hygienic researches, tuberculosis and BCG vaccination, followed by a chapter on developments since

1933. No undue claims are advanced. It is affirmed that BCG is harmless and that the accumulating facts indicate its value. Calmette himself said in effect that only the future can determine what the social benefits from BCG will be. At the end are listed Calmette's publications according to subjects. The book is a notable addition to the biographies of men of science. It is a worthy record of the achievements and personality of a faithful worker in the school of Pasteur.

Shock: Blood Studies as a Guide to Therapy. By John Scudder, M.D., Med.Sc.D., F.A.C.S., from the Surgical Pathology Laboratory of the College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, \$5.50. Pp. 315, with 60 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1940.

The elaborate format of this book seems disproportionate to its content. Parsimonious economy of space alternates with profligate waste of it. A historical summary and review of all preceding work on shock is compressed into eight pages, in which 280 references are cited. Toxemia as a cause for shock is presented and refuted in thirty lines. Citations of authors are substituted for analysis of evidence. Sixteen pages is devoted to potassium and four to all other chemical variations. Stripped of titles, tabulations and figures, the textual matter in parts I and II would fill about forty-five pages, 7 inches to the page. This portion contains 103 full page diagrams, figures, graphs or tabulated case histories in minute detail, twenty-one part page figures or tables, and twenty-one blank pages for readers' notes. In part III, thirty-eight pages is used for listing authors chronologically with a line or two summarizing the contribution: "Dale, 1910, Histamine the cause of shock"; "Cannon, 1917, Reduction of alkaline reserve in shock." The reader receives no aid in evaluating and correlating these fragments. The remainder of the book, pages 237-315, consists of bibliography and index.

The origin and mechanism of shock are not discussed coherently. Isolated statements indicate that the author does not support either of the current hypotheses. A new conception, based on chemical alterations of the blood with vasoconstriction as a fundamental factor, is suggested. No attempt is made to correlate this idea with known physiologic reactions or with the pathology of shock. Hemoconcentration, shown by specific gravity, is emphasized as an early sign, but its possible relation to endothelial permeability is not mentioned. "Changes in the specific gravity of the blood measure changes in vasoconstriction." Hyperpotassemia is explained as indicating profound cellular injury. The data show that hemoconcentration precedes the hyperpotassemia. This fact would indicate that the latter is a secondary feature rather than a prime causative factor. Valuable practical features of this book are hemoconcentration as an early sign and the author's experiences in treatment. A reader seeking information concerning the origin and nature of shock will be disappointed.

Experimentelle Untersuchungen über die spontanen Veränderungen des Blutes in Vitro. Hinsichtlich Suspensionsstabilität, Komplementaktivität, und Antithrombinkfunktion. Von Bengt Bergenhem. Acta pathologica et microbiologica Scandinavica Supplementum XXXIX. Paper. Pp. 251, with 50 illustrations. Uppsala: Almqvist & Wiksells Boktryckeri-A.B., 1938.

This monograph is divided into three major sections: (1) suspension stability of red blood cells, (2) complement activity and (3) antithrombin function. The introductory remarks are devoted to the earlier work of Fahraeus and the author on the suspension stability of red blood cells. The main purpose of the present investigation was to study further the "stabiliserende substanz" which is adsorbed by red cells when serum or plasma is heated to body temperature and thus inhibits the aggregation tendency. This substance is considered identical with lysolecithin. Chapter I is devoted to the historical background of the problem. Chapter II deals with material and methods. In this section the author discusses the influence of defibrination and substances which prevent coagulation on the stabilization process, the morphologic changes of the red cells, the stabilizing process in serum and plasma, the stabilization process and splenic function, and the loss of the stabilizing process in serum and plasma through shaking. Chapter III considers the relation of complement to the stabilization process. Chapter IV deals with the coagulation process, the parallel between the destruction of the red cell aggregation and coagu-

lation enhancing properties of the serum, and antithrombin function of the serum. The author concludes that, with increasing temperature, coagulation activity is paralleled with the decrease of the erythrocyte aggregation. Chapter v includes discussions on saponin hemolysis and the action of tetanotoxin on red cell hemolysis. Finally, the author summarizes his data contained in all the preceding chapters. The work is highly theoretical but should be of provocative interest to hematologists and those interested in hemolysis and hemagglutination.

Gardiner's Handbook of Skin Diseases. Revised by John Kinnear, T.D., M.D., M.R.C.P., Physician for Diseases of the Skin, Dundee Royal Infirmary, Dundee. Fourth edition. Cloth. Price, \$3.50. Pp. 239, with 70 illustrations and 16 colored plates. Baltimore: William Wood & Company, 1939.

In this revision the aim has been to provide a hand book for the general practitioner and medical student and to give an adequate description of the common diseases of the skin with brief reference to the rarer disorders. Only those measures which have proved useful in routine practice are discussed under treatment. The illustrations are good. The material of the book is well classified in the table of contents. The chapter on toxic dermatoses is well done and contains a good discussion of the subject of "sensitization." Sulfanilamide is briefly discussed in the treatment of pemphigus. This brief textbook is good and should adequately serve its purpose as a "hand book for the general practitioner and medical student."

The British Encyclopaedia of Medical Practice Including Medicine, Surgery, Obstetrics, Gynaecology and Other Special Subjects. Surveys and Abstracts 1939. Cumulative Supplement 1939. Under the General Editorship of Sir Humphry Rolleston, Bt., G.C.V.O., M.D. Publishing Editor: Adam Clark, L.M.S.S.A. Sub-Editor: G. Faulkner, D.Sc. Cloth; Boards. Price, \$9. Pp. 605, with 33 illustrations; 170. Toronto & London: Butterworth & Co., Ltd., 1940.

Supplementary to the British Encyclopaedia of Medical Practice, which has been regularly reviewed in these columns, comes a new volume of Surveys and Abstracts and another volume called Cumulative Supplement. The Critical Surveys include authoritative reviews of certain branches of medical science, particularly one on the state and national health by Sir Arthur MacNalty, chief medical officer of the Ministry of Health, London. Others concern general surgery, pediatrics, diseases of the blood-forming organs and other special medical fields. Following the Critical Surveys are discussions of advances in the field of drug therapy, and finally at least half of the volume is devoted to abstracts of medical literature. The price of the volume being considerable, one questions its desirability as a permanent addition to a library, since much of the material it contains is obviously ephemeral. In order to keep The British Encyclopaedia of Medical Practice abreast of progress it has been decided to publish an annual supplemental service planned to present new medical information which has become available since the publication of the original work, the idea being that one reads first the articles in the original twelve volumes of the encyclopedia and thereafter follows with the material under the various headings in the Cumulative Supplement. The selection of the abstracts has been excellent, since it might be said that there is hardly one of them which does not provide useful information.

Manual of Dermatology. By Carroll S. Wright, B.S., M.D., Professor of Dermatology and Syphilology, Temple University School of Medicine, Philadelphia. Cloth. Price, \$4. Pp. 376, with 138 illustrations. Philadelphia: Blakiston Company, 1940.

This manual was written chiefly for medical students and general practitioners of medicine. The illustrations have been excellently reproduced on good paper by the publishers, and the text is printed in clear legible type. Sulfanilamide, nonspecific protein and vitamin therapy are briefly discussed. Parallel differential diagnostic tables are given in many entities, which should be of great value to one inexperienced in dermatologic diagnosis to help properly classify an entity. The sections on tuberculosis, syphilis and diseases due to vegetable parasites are well done and well illustrated. As a compact volume the book admirably serves its purpose as a small text or reference book to be used in connection with clinic and class work and to be complemented by the larger textbooks when more lengthy discussions of a cutaneous entity or bibliography is desired.

Miscellany

TOTAL OF SUICIDES IN THE UNITED STATES EXCEEDS 300,000 FOR 1920-1938

Suicides in the United States totaled more than 300,000 during nearly two decades covered in a report for the years 1920 to 1938 inclusive just issued by the Division of Vital Statistics in the U. S. Bureau of the Census. The exact total was 300,580 suicidal deaths.

The death rate for suicides ranged from 10.2 per hundred thousand of estimated population in 1920, the first year covered in the report, to 15.2 per hundred thousand of estimated population in 1938. The rate for 1938 was the highest since the

Deaths by Suicide and the Rate per Hundred Thousand of Estimated Population in 1938

Area	Number	Rate
Registration area	19,802	15.2
Alabama	220	7.6
Arizona	89	21.6
Arkansas	174	8.5
California	1,874	30.5
Colorado	206	19.2
Connecticut	272	15.6
Delaware	44	16.9
District of Columbia	143	22.8
Florida	264	15.8
Georgia	305	9.9
Idaho	97	19.7
Illinois	1,271	16.1
Indiana	594	17.1
Iowa	418	16.4
Kansas	292	15.7
Kentucky	309	10.6
Louisiana	179	8.4
Maine	152	17.8
Maryland	276	16.4
Massachusetts	590	13.3
Michigan	730	15.1
Minnesota	420	15.8
Mississippi	147	7.3
Missouri	633	15.9
Montana	103	19.1
Nebraska	236	17.3
Nevada	36	35.6
New Hampshire	94	18.4
New Jersey	696	16.0
New Mexico	47	11.1
New York	2,248	17.3
North Carolina	336	9.6
North Dakota	75	10.6
Ohio	1,274	18.9
Oklahoma	258	10.1
Oregon	221	21.5
Pennsylvania	1,397	13.7
Rhode Island	73	10.7
South Carolina	126	6.7
South Dakota	74	10.7
Tennessee	317	11.0
Texas	728	11.8
Utah	63	12.1
Vermont	59	15.4
Virginia	378	14.0
Washington	444	26.8
West Virginia	247	13.2
Wisconsin	527	18.0
Wyoming	46	19.6

heavy depression period of 1930 to 1933 inclusive. The highest rate for all years covered in the report was 17.4 in 1932. The next highest rate was in 1931 with 16.8. The rate for 1933 was 15.9 and for 1930 it was 15.7.

Of the states, Nevada reported the highest suicide rate per hundred thousand of estimated population in 1938 with 35.6; South Carolina reported the lowest rate with 6.7. In total number of suicides in 1938, New York led all the states with 2,248, while Nevada reported the smallest number with thirty-six suicides. California ranked second in total number of suicides in 1938 with 1,874, Pennsylvania third with 1,397, Ohio fourth with 1,274 and Illinois fifth with 1,271 suicidal deaths.

Death totals by suicide and the rate per hundred thousand of estimated population for the forty-eight states and the District of Columbia 1938 are given in the table.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Act: Melanoma Resulting from Mole Irritated by Sand and Ashes an Accidental Injury.—In the course of his employment the workman for a period of about one month operated a machine which made building blocks from ashes, sand and cement. Some sand and ashes invariably fell into his shoes. While at work on July 15, 1936, he felt a severe pain at the site of a pigmented mole, about one half inch (1.25 cm.) in diameter, which he had on "the outer aspect of his instep, just above the little toe" of his left foot. Later that afternoon he noticed that his left sock was stained with blood and that the mole appeared to have been scratched "like the ashes irritated it a little bit." The mole was sore and caused him to limp somewhat, but he continued to work. About four weeks later, some time in August, the mole began to "ooze" and, on the advice of the physician whom he consulted, he was hospitalized for three days. It was discovered that the mole had developed into a malignant tumor, a melanoma, and it was "surgically removed." Six weeks later he was again hospitalized and, because of objective evidence that the disease had spread, "another operation was performed upon the foot and leg as far as the groin." He was released from the hospital thirty-eight days later. He returned to work in January 1937 and was assigned light work. He was denied compensation under the workmen's compensation act of New Jersey by a referee of the workmen's compensation bureau and he appealed to the courts, the case ultimately reaching the Court of Errors and Appeals of New Jersey. Pending the appeal the workman died, presumably from the melanoma.

Compensation was denied the workman by the workmen's compensation bureau and by the lower courts on the theory that since the workman's ailment arose from a "constant irritation of the mole" it was an occupational disease and as such was not compensable under the New Jersey workmen's compensation act, which provides compensation only for a personal injury by accident arising out of and in the course of employment. The Court of Errors and Appeals, however, could find in the record no evidence that there was "constant irritation of the mole" prior to July 15, 1936, nor could it agree with the conclusion of the workmen's compensation bureau and of the lower courts that the testimony did not establish "accidental injury at any time." In the judgment of the court, the evidence did establish (1) that the claimant obviously suffered injury on July 15, which was manifested by pain, limping, bleeding of the mole and the scratch which appeared thereon and (2) that sand and ashes were present around the mole when the injury occurred. The impinging of the sand and ashes on the mole constituted, as all of the medical witnesses agreed, the application of traumatic force, if in the instant case that element is necessary to make out an injury by accident under the workmen's compensation act. While there may have been continued irritation of the mole from July 15, the date when the workman was first injured, to the time in August when he consulted a physician, that did not make the injury any less a compensable injury. If, for example, at a given time sand had struck and lacerated the cornea of the workman's eye, no one would contend that it was not an accidental injury even though previously sand had daily gotten into his eye but had done no damage other than to collect around the margins of the eyelids. In principle there is no defensible distinction between this supposititious case and the instant one.

An injury or death, said the court, to be compensable under the workmen's compensation act must have arisen from accident out of and in the course of employment. Here admittedly the injury arose out of and in the course of the employment, but was there an accidental injury? To be compensable it is not necessary that an accidental injury be the result of traumatic force. The fact that the injury was accidental may legitimately be inferred from circumstantial evidence. An accident is "an unlooked-for mishap or untoward event which is not expected or designed" or "an unintended or unexpected occurrence which

produces hurt or loss." It is clear that the term "accident" is used in the act, and should be so considered, in its ordinary, popular and accepted sense. An "accident," therefore, need not be due to any extraneous event or occurrence. Reverting to the testimony, said the court, there was no claim by the employer that "cancer" was already present at the time of the injury on July 15, or that "cancer" would have resulted in any event apart from employment. There was ample testimony of an unexpected occurrence resulting in an injury on July 15. Furthermore, there was an undisputed causal connection between the injury of July 15 and the fatal result. Also no proof was advanced that the mole was ever irritated before the date in question. The medical testimony showed that the impinging of the sand on the mole and the irritation caused thereby on July 15 produced the melanoma. Accordingly, the court held that the disability and resulting death of the workman was the result of an accidental injury and that the workman's widow was entitled to compensation.—*Bollinger v. Wagaraw Bldg. Supply Co. (N. J.), 6 A. (2d) 396.*

Lead Poisoning Following Short Exposure to Paint Spray Not an Accidental Injury.—Bailey, in the course of his employment as a laborer for Salt Lake City, started, March 24, 1935, painting trucks with a paint spray. No mask was furnished him. He became ill April 10 and died April 15 from lead poisoning, allegedly resulting from inhalation of the vaporized paint. The industrial commission of Utah denied his mother, the plaintiff, compensation under the Utah workmen's compensation act on the ground that the workman's illness was an occupational disease and was not compensable under the Utah act, which provides compensation only for injury or death "by accident arising out of or in the course of" employment. Subsequently the mother brought suit against the city under the so-called wrongful death statute, which authorizes an action against a tortfeasor "Except as provided in [the workmen's compensation act] . . . when the death of a person . . . is caused by the wrongful act or neglect of another . . ." The trial court sustained a demurrer interposed by the city on the assumption that the action was barred by the workmen's compensation act. The plaintiff then appealed to the Supreme Court of Utah.

The main question to be determined by the Supreme Court was whether Bailey's ailment was an occupational disease or an accidental injury, for the court assumed that if the workman had contracted an occupational disease the action of the trial court was in error and that if the workman's ailment was an accidental injury the ruling was correct. The court then considered cases holding that where injury is traceable to a particular time, place and circumstance it is an accidental injury but where the condition arose gradually and cumulatively from the character of the employee's work it is an occupational disease. If the illness, said the court, is one commonly recognized as incident to the particular occupation, it is an occupational disease. The time taken for the effects of the occupation to become serious is not the governing factor. Some people are less resistant to imperfect conditions than others. To stress length of time as a basis of determining the accidental nature of an illness is to adopt a rule which may, in many cases, be governed by the person's bodily resistance. If such a rule were adopted, the dividing line between an occupational disease and an accidental injury would become extremely hazy as the periods of time for each approached unity. The fact that the workman in this case succumbed in a comparatively short time to lead poisoning from inhaling the vapor was not conclusive that his illness was accidental.

In deciding a case of this kind, continued the court, we should ascertain first whether the illness is one commonly recognized as incident to the usual performance of the occupation. If it is not, then the question of an occupational disease is ended. If it is incident to such performance, then we should ascertain whether some definite unexpected or unusual circumstance took place—something that interjected itself into the usual course of the performance of the occupation. And, finally, we should ascertain whether or not this circumstance, if one there be, accelerated or changed the effect of the otherwise resultant occupational illness. If it did, then that illness was the result of an accidental injury. But, from the fact that an unexpected

or unusual circumstance may accelerate an illness, we must not reason backward and say that the shortness of the period of exposure to imperfect conditions of employment before an illness develops proves that there was some unusual circumstance about the performance of the occupation that made it accidental. The result must be traceable to a particular circumstance, which should be identified as to time and place and not merely inferred. In the instant case the workman suffered an illness which he did not know might follow from breathing the vaporized paint. So far as the records showed, no circumstance occurred in the performance of his employment which differed from the usual performance of such labor of painting with a spray gun. The city's failure to give him a mask, whether deliberate or through carelessness, was not accidental. The unusual or unexpected circumstance which classifies an illness as accidental must occur in the events leading up to the illness. From the fact that Bailey did not know what would be the effects on his health of the performance of his employment, we must not conclude, said the court, that his resultant illness, which to others with superior knowledge would be an occupational disease, was an accidental injury. Lack of knowledge of results is not the circumstance to which the illness must be traceable. That circumstance must lie in the causal connection between the occupation and the illness.

The Supreme Court held, therefore, that action under the wrongful death statute was maintainable, since Bailey's injury and death were not compensable under the workmen's compensation act. Accordingly, the judgment of the lower court sustaining the demurrer and dismissing the action was set aside and the case remanded.—*Young v. Salt Lake City (Utah)*, 90 P. (2d) 174.

Optometry Practice Act: Legality of Corporate Practice; Optometry Not a Learned Profession.—Lansburgh and Bro., a corporation operating a department store in Washington, D. C., leased space in the store to the Buhl Optical Company, a corporation, in which to conduct a so-called optical department for the examination of eyes and the sale of eyeglasses and other optical goods. The optical company agreed to pay as rent a sum equal to 20 per cent of the gross volume of business done therein and to spend a sum equal to at least 5 per cent for advertising. The department store agreed to collect and pay over to the optical company all receipts from credit sales made in the "optical department" after deducting the rent and the salaries of the employees in that department. Although these employees were paid by the department store, they were hired by the optical company, were subject to its exclusive control and were not subject to the direction or supervision of the department store. The "optical department" was placed in charge of an optometrist, duly licensed in the District of Columbia, who was employed on a salary basis and paid by the department store.

The plaintiffs, licensed optometrists, brought suit in the district court of the United States for the District of Columbia to enjoin the department store and the optical company, the defendants, from engaging in the practice of optometry. The plaintiffs alleged (1) that optometry is a learned profession and its very nature prohibits a practitioner thereof "from any affiliation or connection with a corporation or non-optometrist" and (2) that the optometry practice act of the District of Columbia specifically prohibits the employment of duly licensed optometrists by a corporation or non-optometrist. The district court, however, held that optometry is not a learned profession comparable with law, medicine and theology but is in its nature empirical and "essentially a mechanical art which requires skill, manual dexterity, and a knowledge of the use and application of certain mechanical instruments and appliances designed to measure and record the errors and deviations from the normal which may be found in the human eye." The court refused to grant the injunction sought and so the plaintiffs appealed to the United States Court of Appeals for the District of Columbia.

In *United States v. American Medical Association* (District of Columbia), 110 F. (2d) 703, said the Court of Appeals, this court pointed out that in the District of Columbia the practice of medicine, which is subject to licensing and regulation, may not lawfully be subjected to commercialization and exploitation, and that a corporation is engaged unlawfully in the practice of

medicine when it employs licensed physicians to treat patients, itself receives the fee and has for its main object the profit motive. This rule, however, does not apply to the practice of optometry. Notwithstanding the fact that the optometry practice act prescribes certain educational and professional qualifications which applicants for licensure must meet, optometry is not "one of the learned professions." In so holding the court quoted with approval from E. E. Arrington's *History of Optometry* (1929), p. 24:

Ocular refraction is not, and never has been, a part of medicine, either by inheritance, basic principles, development or practice. It is an applied arm of optical science, resting upon the work and discoveries of physicists and opticians through the ages, down to modern times. It does not treat the eye, whether in health or disease, but adapts the light waves which enter the eye, in accordance with optical principles, so as to produce focused and single vision with the least abnormal exertion on the part of the eye. And, finally, its distinction from and independence of medicine have been affirmed by supreme court decisions in every case in which the question has been brought up for adjudication.

It was the opinion of the court that the optometry practice act neither requires nor contemplates that an optometrist shall be a graduate physician nor that he shall, like an oculist or ophthalmologist, diagnose or treat diseases of the eye. In actual practice, the optometrist only measures the refractive abnormalities of the eye and prescribes and sometimes grinds lenses to correct them. While there are cogent reasons for preventing the practice of law and medicine through corporations, no such reasons are apparent with respect to the practice of optometry. The professional service required of a physician or a lawyer creates a relationship of trust and confidence. The necessary disclosures which the patient or client must reveal to the physician or lawyer create a personal relationship which cannot exist between patient or client and a profit-seeking corporation. The universal recognition of a confidential association between the physician and the lawyer and those who engage their services justifies the rule that their allegiance must be wholeheartedly to the patient or the client and not to another. In the case of optometry, however, while it may be a profession in the colloquial sense of the term, there is no more reason to prohibit a corporation from employing licensed optometrists than to prohibit similar employment of accountants, architects or engineers. Furthermore, the court could find nothing in the optometry practice act itself to prohibit corporations from employing licensed optometrists to perform optometric services. The primary purpose of the act is to insure the rendering of optometric services by competent persons and thus to protect the public from inexperience. That purpose may be accomplished even though the optometrist is employed by a corporation. For the reasons stated, the Court of Appeals affirmed the judgment of the district court denying injunctive relief.—*Silver v. Lansburgh & Bro. et al. (District of Columbia)*, 27 F. Supp. 682; 111 F. (2d) 518.

Society Proceedings

COMING MEETINGS

- American Association of Railway Surgeons, Chicago, Sept. 16-18. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.
- American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.
- American Hospital Association, Boston, Sept. 16-20. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.
- Colorado State Medical Society, Glenwood Springs, Sept. 11-14. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.
- Idaho State Medical Association, Sun Valley, Sept. 11-14. Dr. J. N. Davis, 204 Fourth Ave., East, Twin Falls, Secretary.
- Kentucky State Medical Association, Lexington, Sept. 16-19. Dr. A. T. McCormack, 620 South Third St., Louisville, Secretary.
- National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
- Oregon State Medical Society, Eugene, Sept. 4-7. Dr. Morris L. Bridgeman, 1020 S.W. Taylor St., Portland, Secretary.
- Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
- Virginia Medical Society of, White Sulphur Springs, W. Va., July 29-31. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.
- Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
- West Virginia State Medical Association, White Sulphur Springs, July 29-31. Mr. Joe W. Savage, Public Library Bldg., Charleston, Executive Secretary.
- Wisconsin State Medical Society of, Milwaukee, Sept. 18-20. Mr. J. G. Crownhart, 110 East Main St., Madison, Secretary.
- Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia 199:749-892 (June) 1940

- *Antienzymatic Nature of Sulfanilamide's Bacteriostatic Action. R. R. Mellon, A. P. Locke and L. E. Shinn, Pittsburgh.—p. 749.
Effect of Sulfanilamide Compounds on Endocarditis. R. H. Major, Kansas City, Kan.—p. 759.
Sickle Cell Anemia in a White Family. L. Greenwald and J. B. Burrett, New York.—p. 768.
Effect of Storage on Prothrombin Content of Citrated Blood. J. Reinhold, Eleanor H. Valentine and L. K. Ferguson, Philadelphia.—p. 774.
Role of Water Balance in Clinical Manifestations of Allergy. R. A. Kern, Philadelphia.—p. 778.
Electrocardiographic and Serum Potassium Changes in Familial Periodic Paralysis. H. J. Stewart, J. J. Smith and A. T. Milhorat, New York.—p. 789.
Prognostic Significance of Right Axis Deviation in Arteriosclerotic and Hypertensive Heart Disease. M. J. Klainer, Boston.—p. 795.
*Treatment of Alcoholism by Establishing a Conditioned Reflex. W. L. Voegtlin, Seattle.—p. 802.
Studies on Purified Antigen from Brucella. P. Morales-Otero and L. M. González, San Juan, Puerto Rico.—p. 810.
Experimental Hypertension in Nephrectomized Parahibiotic Rats. W. A. Jeffers, M. A. Lindauer, P. H. Twaddle and C. C. Wolferth, Philadelphia.—p. 815.
Hypertension, Body Build and Obesity. S. C. Robinson, with collaboration of M. Brucer, Chicago.—p. 819.
Effect of Large Doses of Insulin on Glucose Tolerance. J. W. Appel and J. Hughes, Philadelphia.—p. 829.
Effect of Added Carbohydrate on Stabilized Insulin-Treated Diabetics. M. Fabrykant, Paris, France, and H. J. Wiener, New York.—p. 834.
*Incidence of Neuropathy in Pellagra: Effect of Cocarboxylase on Its Neurologic Signs. F. H. Lewy, Philadelphia; T. D. Spies and C. D. Aring, Cincinnati.—p. 840.
Cerebral Carbohydrate Metabolism During Deficiency of Various Members of Vitamin B Complex. H. E. Himwich, Albany, N. Y.; T. D. Spies, Cincinnati; J. F. Fazekas and Sarah Nesin, Albany, N. Y.—p. 849.
Porphyrinuria in Pellagra. L. A. Rosenblum and N. Jolliffe, New York.—p. 853.

Bacteriostatic Action of Sulfanilamide.—Mellon and his co-workers discuss the amount of hydrogen peroxide per unit of bacterial substance necessary for bacteriostasis in the presence of sulfanilamide and the dependence of bacteriostasis on an adequate supply of oxygen. A progressive decrease in oxygen tension of the cultures is accompanied by a decrease in the bacteriostatic effect caused by sulfanilamide. The fact that such diverse species of bacteria as hemolytic streptococci, pneumococci, gonococci, meningococci and *Bacillus coli* produce hydrogen peroxide and that they are all rather highly sensitive to its toxic effect offers plausible explanation for the broad therapeutic coverage of the drug. When the hydrogen peroxide-producing power of the pneumococcus is suppressed, it is no longer vulnerable to the drug sulphyridine. Enzymes other than catalase are affected either directly by the drug or possibly secondarily by the toxic action of accumulated hydrogen peroxide. Peroxydase is adversely affected and certain dehydrogenases are inactivated. Antienzymatic conception is sponsored without, however, limiting the effect to a single enzyme. The conception does not exclude toxin inactivation as supported by Carpenter. Toxins are notoriously susceptible to oxidation. The oxidativ-enzymatic theories are rather generally supported by clinical evidence. Virtually all the infections decisively influenced are of aerobic nature. An exception is the staphylococcus. The highly reducing nature of staphylococcal lesions is regarded as preventing the oxidation of sulfanilamide that conditions its antienzymatic effect. Whether this explanation is adequate will perhaps be apparent when more is known of the action

of the sulfathiazoles, which appear effective against this organism. It is also possible that the protein degradation products present in abscesses may condition the action of the drug in accordance with mechanisms that are not anaerobic. The decisive action of sulfanilamide against *Bacillus coli* in urine but not in peptone-containing mediums leaves no doubt of the importance of environmental factors. In fact, they may result in multiplying the effect of the drug many times. This potentiating action is particularly conspicuous when antiserums are combined with the drug. The effect of bacteriostasis against pneumococci *in vivo* is to bring about their "dissociation" into culture phases, whose principal metabolic functions, including hydrogen peroxide formation and virulence, are so critically suppressed that the organisms fall easy prey to the destructive action of the phagocytes.

Conditioned Reflex for Treatment of Alcoholism.—During the last four years Voegtlin has treated 685 cases of chronic alcoholism by utilizing emetine and apomorphine to elicit the unconditioned reflex of nausea and vomiting. Aversion to alcohol is developed during a number (usually from five to seven) of sances or treatments with rest periods between. No food, except liquids, and no sedative drugs are given for at least twelve hours before each treatment. Alarming though not dangerous collapse may follow the injudicious administration of the medication. The treatment room is soundproofed to avoid extraneous stimuli. The lighting is subdued with the exception of the treatment table with its array of liquors, which is "spot lighted," causing the sight of liquor to become an element of the conditioned stimulus. Similarly, by forcing the patient to smell deeply of various liquors the olfactory sense may also be utilized. Usually this aversion to sight and smell is sufficient to cause the patient to avoid alcohol without the more dangerous experiment of tasting liquor. Since the conditioned stimulus is specific, it is necessary to use every conceivable type of liquor. A fall in systolic blood pressure below 100 is an indication for rest and ephedrine medication until a near normal level is again reached. It is well to mention casually to the patient that the medication (emetine and apomorphine) is merely a stimulant to support him during the ensuing violent nausea and also suggests that the drinking of the liquor causes the acute illness. Experience alone will enable one to judge the exact moment when the emetine nausea will begin (usually from two to eight minutes) and consequently the exact moment when the first drink of liquor should be offered. This first offering of liquor should be given within several seconds of the onset of nausea and it should never be withheld until nausea or salivation has appeared. If an error in timing has been committed, the onset of nausea may be hastened by administering from 1 to 2 grains (0.065 to 0.13 Gm.) of emetine orally in whisky. Following the onset of nausea all types of liquor are forced on the patient, making certain that each empty glass is smelled deeply. Warm water is given frequently in order to afford easy emesis and to avoid retching. After emesis is completed the treatment is repeated until the nauseant effect has begun to wane. The stomach is then thoroughly emptied and washed by means of the Ewald tube with warm water. The patient is left in the treatment room until the pilocarpine diaphoresis has ceased. The stomach must be emptied promptly if a patient is unable to regurgitate. Absorption of alcohol to the point where an effect is noticed by the patient will vitiate the entire treatment. Contraindications to the treatment are the cardiovascular-renal syndrome, hepatic cirrhosis with or without esophageal varices, hernia (unless guarded), active peptic ulcer, recent hematemesis and active psychosis. The exact status of 538 of the patients treated is known. During each six month period for the last four years the proportion of sobriety has been remarkably constant, varying only between 62 and 69 per cent. While the proportion of abstinence for the six months immediately following treatment is 97.3 per cent, the proportion during the second six months is only 65.7 per cent. If a relapse does not occur during the first year, its subsequent occurrence is not great. A conservative expectation of 64.3 per cent of total and permanent cures is obtained from an average of eight six month periods. By a "cure" is meant total and permanent abstinence from alcohol of all types. The percentage of

abstinence among women patients was found to be only 57. Relapses were more common among wine than beer drinkers and least frequent among users of distilled liquors. Many of the patients who have relapsed have presented themselves for retreatment. The prognosis in these patients seems poorer. Delirium tremens developed in only fourteen. Twenty-one patients were admitted in acute delirium. Only one of these thirty-five patients with delirium tremens died. This occurred before treatment was instituted. The mortality of the entire series of cases receiving the complete treatment was a single death (0.14 per cent) due to cardiac failure. Laboratory studies show that while 36.8 per cent of patients had albuminuria on admission only 3.9 per cent did on discharge.

Coccarboxylase for Neuropathy in Pellagra.—Lewy and his associates determined the incidence of neuropathy among fifty pellagrins (thirty female and sixteen male patients between 18 and 66 years of age) and four children between 8 and 13 years of age. More than three fourths of the patients were regarded as having mild or moderately severe pellagra. The preponderance of such cases is explained by the fact that only ambulatory patients were examined. Clinical examination revealed that 75 per cent had polyneuropathy of the motor and sensory nerves, 20 per cent had extrapyramidal signs (one half of these showed mild parkinsonism) and 12.5 per cent had tremor and pyramidal tract signs. Intravenous administration of 50 mg. or more of phosphorylated thiamine (coccarboxylase) to nine of these pellagrins was followed by quantitative improvement in the electrical irritability of a number of muscles of seven of them. Improvement also was observed in the pupillary and corneal reflexes and in the sensitivity to touch and pinprick. These indexes often became normal within one to four hours after injection, and improvement was maintained for from one to five days. The patient then tended to regress and eventually returned to the condition preceding treatment. The clinical effect of coccarboxylase was found to be identical with that of thiamine (vitamin B₁) studied previously. The chemical changes in the blood following administration of coccarboxylase paralleled the clinical neurologic improvement. These observations confirm the premise that the neuropathy which is common among pellagrins is caused by a deficiency of vitamin B₁. Patients who retained most of the injected coccarboxylase improved readily, while those who were unable to retain it showed little or no improvement. The administration of synthetic riboflavin was not followed by a change of the neurologic signs.

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 *Treatment of Endocervicitis with Carbon Dioxide Snow (Dry Ice). G. Weitzner, New York.—p. 620.
 Transurethral Resection for Cancer of Prostate. C. D. Creevy, Minneapolis.—p. 646.

Diaphragmatic Hernia in Children.—Hartzell reviews sixty-eight cases of diaphragmatic hernia occurring in children 10 years of age or less. There was a total mortality of 32 per cent. Nineteen patients died shortly after operation and are classed as operative deaths. Three died after leaving the hospital, one two months and one six months later, of recurrence which resulted in obstruction. Neither was reoperated on. In the third case the hernia recurred in six months, and the patient died after a second operation. There were two more recurrences. These two patients were operated on again. One made a satisfactory recovery and has remained well. The hernia recurred twice more in the other patient and following the third operation he has remained well. Cyanosis, dyspnea and vomiting are the most common symptoms in children less than 1 year of age, while in older children vomiting, pain and colic are the most common complaints. In children less than 1 year old the dominant symptoms result from cardiac and pulmonary embarrassment, while in older children they result from partial obstruction of the gastrointestinal tract. In any case showing these symptoms, the physical examination may reveal tympany on percussion, dextrocardia, dullness to flatness on percussion and absent or diminished breath sounds on the involved side; râles, diminished excursion on the involved side, retraction of the abdomen, an epigastric mass and a rapid heart beat. No diagnosis can be considered complete without a roentgenogram. In sixty of the sixty-eight cases the x-ray examination was used either to make or to confirm a diagnosis. In five of the eight cases not submitted to x-ray study the diagnosis was definitely missed. The diagnosis of diaphragmatic hernia is more frequently made in the male than in the female, and the operative mortality is higher in the latter. The most common type is the false hernia through the left diaphragm. A diaphragmatic hernia constitutes a menace to life. Except in the case of a symptomless infant less than 1 year of age, a definite diagnosis of a diaphragmatic hernia should be followed by immediate surgical intervention. The abdominal approach is usually the best. No one should favor the combined approach unless necessity demands it. The anesthetist should always be prepared to administer a positive pressure anesthesia if the need arises. Positive pressure anesthesia is indicated in the false hernia in which there is no sac. The truth of this is well verified by the higher mortality in the group operated on via the abdominal approach without the benefit of positive pressure anesthesia. The 7.7 per cent mortality in those operated on by the abdominal route given proper anesthesia is satisfactory. A study of the mortality with relation to the age of the patient reveals that it is definitely higher during the first year of life. The twenty-four cases in the present series occurring under 1 year of age were all congenital, and the mortality was 50 per cent. After the first year the

mortality dropped to 22.7 per cent. In the congenital and acquired cases it was about four times as great as in the traumatic cases.

Solid Carbon Dioxide for Endocervicitis.—Weitzner applied topically a rod of solid carbon dioxide to the cervical canal for from sixty to ninety seconds in the treatment of 325 cases of endocervicitis. The first patient was treated in May 1934 and the last in December 1935; 70 per cent of the patients required only one treatment for a cure (cases with erosion responded more readily to the treatment), 15 per cent required two treatments and 15 per cent were treated three or more times. No postoperative sequelae, such as bleeding, inflammation or stenosis of the cervical canal, have been observed after two and a half years of follow-up. Inspection of the treated areas twenty-four hours after treatment shows them to be covered by a grayish pseudomembrane. Seven days after treatment the areas are no longer so covered. The cervix bleeds readily to touch. Biopsies taken at this stage show areas of necrosis still present, but in general the picture is one of early regeneration, especially in the region of the stratified squamous epithelium. Inflammatory changes are absent. From ten to seventeen days after treatment macroscopic signs of healing are visible. From three to four weeks after treatment the entire area of the erosion is covered by stratified epithelium. Eight weeks after treatment cervical biopsy shows complete cure. In thirty-one of 111 cases atypical cells were found on microscopic study in atypical arrangement, apparently invading the surrounding tissue. These cells resembled the earliest stages of cervical malignant changes to such an extent that treatment was suspended pending further study and follow-up. On the basis of 201 biopsies taken from the cervixes showing the atypical cells the following statements are made: 1. There were erosions in all cases prior to treatment. 2. The number of treatments had no influence on the development of atypical cells. 3. The atypism was observed as early as one week after treatment. 4. The duration of the atypism ranged from three months to more than two and a half years. 5. Cases with atypical cells showed macroscopically a perfectly smooth normal cervical surface. Berenblum concluded from his experiments that solid carbon dioxide has no carcinogenic properties either for animals or for human beings. Thus it appears that these nests of atypical cells have nothing in common with true malignant changes. They may be regarded as signs of increased activity of the stratified squamous cell epithelium in a healing erosion.

American Journal of Tropical Medicine, Baltimore

20:345-462 (May) 1940

Discussion of Etiology of Sprue. E. B. Vedder, Washington, D. C.—p. 345.

*Internal Autoinfection in Human Strongyloidiasis. E. C. Faust, New Orleans, and A. de Groat, Little Rock, Ark.—p. 359.

*Treatment of Oxyuriasis. J. S. D'Antoni and W. Sawitz, New Orleans.—p. 377.

The Mosquitoes of Costa Rica. H. W. Kumm, San Jose, Costa Rica, C. A.; W. H. W. Komp and H. Ruiz.—p. 385.

Further Observations on Comparative Susceptibility of Nearctic and Neotropical Anophelines to Coincigenous Strains of Plasmodium falciparum. M. F. Boyd, Tallahassee, Fla., and D. M. Jobbins, Panama City, Republic of Panama.—p. 423.

Study of Winter Activities and Hibernation of Anopheles Quadrimaculatus in the Tennessee Valley. E. H. Hinman and H. S. Hurlbut, Wilson Dam, Ala.—p. 431.

Preservation of Yellow Fever Virus. J. P. Fox and S. Gard, New York.—p. 447.

Internal Autoinfection in Human Strongyloidiasis.—According to Faust and de Groat, critical examination of the parasitologic and clinical literature indicates that hyperinfection (internal autoinfection) is not only a necessary hypothesis to explain the relatively frequent cases of human strongyloidiasis which have persisted for many years in the absence of external sources for reinfection but is supported by experimental, clinical and postmortem evidence. The case reported in this communication provides additional evidence demonstrating a relatively heavy invasion of the deeper layers of the bowel wall and liver by filariform larvae derived from mother worms situated in the overlying mucosa. Except for a localized eosinophilic response around the migrating worms no cellular reaction was provoked by this invasion. This stands in marked contrast to the picture

of leukocytosis with hypereosinophilia which characterizes the usual case of acute strongyloidiasis. Self infection in strongyloidiasis may result (1) from the perianal invasion of larvae, (2) from the invasion of the mucosa of the lower levels of the bowel by filariform larvae which have originated from sites of infection at higher levels, (3) from the penetration of filariform larvae into the deeper layers of the bowel at the same level where they were produced in the mucosa or (4) from unmetamorphosed rhabditoid larvae massively penetrating through the muscularis mucosae into the deeper layers of the bowel wall. Probably all persons harboring Strongyloides are potential subjects of self infection. The authors stress that self infection with Strongyloides stercoralis may be controlled, or at least measurably reduced, by heeding certain dictums of personal hygiene, by providing adequate nutrition and hemopoietic stimuli. Physicians should be more conscious of the possibility of strongyloidiasis; they should make their diagnosis as early as possible and carry out specific therapy until the infection is eradicated.

Treatment of Oxyuriasis.—D'Antoni and Sawitz studied the efficacy of gentian violet for oxyuriasis patients in an institutional environment. The investigations were made on indigent or orphan children in three institutions in New Orleans. They were apparently healthy white males and females from 3 to 21 years of age but mostly from 11 to 17 years. The diagnosis of oxyuriasis was based on the NIH swab (Hall's cellophane-tipped glass rod) technic. The persons examined were considered free from pinworms only after seven negative NIH swabs. The seven posttreatment swabs were taken within twenty-six days following treatment. In one home 38 per cent of the children (twenty-three girls and thirty-five boys) were found infested with Enterobius vermicularis. Rigid hygienic measures were carried out over a period of six weeks, but a 13 per cent increase in incidence occurred. In another home 97 per cent of 122 boys, and in the third home 81 per cent of twenty-six girls were found infested. Treatment of the infested boys and girls with coated half grain tablets of gentian violet medicinal in varying dosages resulted in a cure of approximately 90 per cent. The untoward symptoms of gentian violet medication were not serious. Vomiting occurred in a high percentage, but its frequency was low when computed on a basis of the total number of doses of the drug. It was found to occur more frequently in females than in males. The authors emphasize the difference between the cure of the individual with gentian violet and the eradication of an infestation in an institution.

American Review of Tuberculosis, New York

41:675-832 (June) 1940

*Results of Extrapleural Thoracoplasty for Pulmonary Tuberculosis. G. N. J. Sommer Jr., Trenton, N. J., and A. A. Ehler, Albany, N. Y.—p. 675.

Tuberculous Tracheobronchitis: A Review. R. S. Jenks, Mount Morris, N. Y.—p. 692.

Routine Bronchoscopy in Tuberculosis. J. C. Sharp and C. B. Gorham, Salinas, Calif.—p. 708.

*Cystic Lungs. S. Diamond, Legion, Texas, and W. R. Durham, Oteen, N. C.—p. 719.

Sulfapyridine in Experimental Tuberculosis: Pathology of Experimental Tuberculosis and of Apparent Toxic Changes in Guinea Pigs Treated with Sulfapyridine. W. H. Feldman and H. C. Hinshaw, Rochester, Minn.—p. 732.

Progressive Primary Tuberculous Complex. M. R. Louria, New York.—p. 751.

Anorectal Tuberculosis. G. H. C. Joynt, London, Ont.—p. 760.

Incidence of Tuberculosis Among Students at Lund University. E. Hedvall, Lund, Sweden.—p. 770.

Tuberculosis Survey of San Bernardino County. E. Bogen, Olive View, Calif.—p. 781.

Case Finding. W. H. Hatfield, Vancouver, B. C.—p. 784.

Medicolegal Aspects of Silicosis. T. C. Waters, Baltimore.—p. 792.

Extrapleural Thoracoplasty and Tuberculosis.—Sommer and Ehler determined the influence of certain conditions on the results of extrapleural thoracoplasty for pulmonary tuberculosis in 177 patients. Seven patients died from causes directly or indirectly connected with operation, one patient committed suicide and thirteen patients died after their discharge to sanatoriums or their homes; 140 patients have closed cavities and sputums negative for tubercle bacilli and fifteen living patients have positive sputum. Of the 176 traced patients 155 are

living, the average length of follow-up being thirty and one half months. Of these living patients 140 have closed cavities and negative sputums. No patient has been considered quiescent unless his sputum has been negative on examinations of concentrated specimens and cultures for at least six months. Twenty-eight patients are classified as apparently cured, fifty-five as arrested, forty as apparently arrested, fifteen as quiescent and two as improved. These two patients are classified as only improved in spite of closed cavities and negative sputums as one is dyspneic and the other is thought by her physician to have a blocked cavity. Ninety-four of the 140 patients with closed cavities and negative sputums are now working full time or part time or are able to work. Only the seventeen patients classified as quiescent or improved remain in sanatoriums. While the size of the pulmonary cavities appears to be of significance in affecting the results of thoracoplasty, more important factors are incomplete operation, contralateral active tuberculosis and early regeneration of resected ribs. The patient's age, duration of tuberculosis, the presence of pneumothorax with or without effusion or empyema and the position of the cavities in the lungs are of relatively little significance.

Cystic Lungs.—Diamond and Durham report ten cases of cystic disease of the lungs. Six of these were encountered within a period of nine months among approximately 1,500 consecutive general hospital admissions. Recent observations seem to indicate that truly congenital cysts are less frequent than was formerly thought. A careful history and frequently repeated examinations often suggest the pathogenesis of acquired cystic disease in individual patients. The structural variations among cystic lungs are as marked as are the differences in their etiology. Cysts may be single or multiple, unilocular or multilocular. They may be present in any part of one or both lungs. The condition occurs about as often in the two sexes. The cysts range in size from tiny sacs to incredibly huge air pockets. Roentgenographically, air cysts appear simply as areas of increased illumination in which normal lung markings are absent. When several are situated close to one another, their condensed septums may appear as very fine straight or curved lines, giving the appearance of a large honeycomb. It is often difficult to distinguish an air cyst from a pneumothorax. It may become necessary to induce a diagnostic pneumothorax to make a diagnosis. The authors have not been able to introduce iodized poppy-seed oil into these cysts through endobronchial catheters. The oil failed to flow beyond one of the larger bronchial radicles, suggesting that the bronchial opening of these cysts must be exceedingly small, in contrast to that present in typical bronchiectatic cavities. Cystic lungs have no distinctive clinical picture and may occur at any age. Many patients are symptom free throughout their lives, the lesion being discovered during a routine physical or x-ray examination. The clinical manifestations may be quite pronounced. The severity of the symptoms in uncomplicated cases apparently is determined by the extent of actual loss of pulmonary tissue and intracystic pressure. As the effective breathing space is encroached on, the patient becomes dyspneic; the greater the reduction of his vital capacity, the more uncomfortable he becomes. This dyspnea, caused by permanent absence of parenchymal tissue, is continuous. Complications, infection of the cyst or its rupture into the pleural space, are relatively rare; when they do occur the clinical picture of the secondary process usually supersedes that occasioned by the cystic disease. The ten patients discussed saw arduous military service during the World War. At the time of their enlistment these men were presumably free of symptoms. Four of the patients had but one cyst and six had more than one. The condition was found in the left lung in two, in the right in two and in both lungs in six patients. The upper and lower thirds of the lungs were involved with approximately equal frequency, the middle thirds less often. Six men gave a history of previous respiratory disease. The four patients with no symptoms attributable to their cystic disease had only a small, solitary cyst. Two patients suffered for years from a persistent, unvarying dyspnea and numerous cysts were present in both. The four remaining patients gave a history of gradually increasing dyspnea. Two of these died; postmortem examination of one demonstrated that cystic disease was the cause of death.

Archives of Dermatology and Syphilology, Chicago 41:1001-1224 (June) 1940

- ***Dermatomyositis:** Study of Forty Cases. P. A. O'Leary and M. Waisman, Rochester, Minn.—p. 1001.
Eczema of Ear Associated with a Diphtheria-like Organism: Report of Case. J. J. Eller and L. H. Kest, New York.—p. 1020.
Superficial Noninflammatory Lesions of the Feet: Demonstration in Sections of a Fungus of the Genus *Actinomyces*. H. Sutherland-Campbell, Los Angeles.—p. 1023.
Whealing Capacity of Skin of Newborn or Young Infant: Report of Experiments. M. B. Sulzberger and R. L. Baer, New York.—p. 1029.
Erysipeloid: Report of Case. R. B. Grinnan and W. B. Martin, Norfolk, Va.—p. 1037.
Eruptions and Photosensitivity Due to Dyed Fabrics. E. Epstein, Oakland, Calif.—p. 1044.
Acute Arthritis Associated with Myocarditis Simulating Acute Lupus Erythematosus: Report of Case. H. C. Gotsbalk and J. T. Wayson, Honolulu, Territory of Hawaii.—p. 1053.
Clavicle Sign of Late Congenital Syphilis: Review of Literature and Report of Six Cases. K. L. Yang, Shanghai, China.—p. 1060.
Erythema Exsudativum Multiforme (Hebra) with Conjunctivitis and Stomatitis. L. Rosenberg and J. Rosenberg, Brooklyn.—p. 1066.
Cases of Familial and of Conjugal Pemphigus Vulgaris: Use of Transfusions of Blood from Cured Patients. S. S. Greenbaum, Philadelphia.—p. 1073.
Erythema of Ninth Day Following Bismuth Therapy for Syphilis. J. L. Grund, Boston.—p. 1076.
Acute Syphilitic Transverse Myelitis: Clinical Study and Report of Case. S. Berman, Northport, N. Y.—p. 1078.
The Sudoriparous Glands: III. Sweat. S. C. Way, San Francisco, and A. Memmesheimer, Essen, Germany.—p. 1086.

Dermatomyositis.—According to O'Leary and Waisman, between 1926 and 1939 forty unquestionable cases of subacute and chronic dermatomyositis were observed at the Mayo Clinic. A history of acute infection (tonsillitis, influenza and sinusitis) antedated the onset of the dermatomyositis in eleven. Recent parturition preceded the disease in three. Chronic diseases, including pulmonary tuberculosis, bronchiectasis, rheumatic fever, recurrent furunculosis and infectious arthritis, were observed in ten others. Adenocarcinoma of the rectum with metastasis to the liver was associated in one case. Dermatomyositis may be heralded by muscular, cutaneous or vasomotor signs. The most common early complaint among eighteen patients was muscular pain and weakness, and in fourteen edema and cutaneous lesions ushered in the disease. In six other cases muscular and dermatologic symptoms were initially combined in the form of eruption (or edema) and weakness, with or without pain. Vasomotor phenomena were observed in two cases before symptoms referable to the skin or to the musculature appeared. The muscular involvement was not regular or constant in sequence. Usually the myositis was characterized by a nearly symmetrical bilateral involvement. The consistency of the muscles may be normal, soft and doughy or tough, firm and fibrous. Muscular atrophy usually developed in cases of longer duration, and dermatomyositis was frequently associated with muscular contractures and "fixed joints." The deep reflexes were occasionally normal, but more often they were decreased or absent. The vital striated musculature (pharynx, larynx, intercostal muscles and diaphragm) was involved and this was an extremely serious complication. Twenty-seven patients experienced dysphagia. Thirteen exhibited vocal changes; hoarseness or altered pitch. Ten patients experienced frank dyspnea. Weakness and tremor of the tongue occurred in six and diplopia was complained of by four. Occasionally cutaneous changes are absent, but in most cases they are prominent and include erythema, edema, pigmentation, sclerosis, atrophy, lupus erythematosus-like efflorescence and poikiloderma atrophicum vasculare. The systemic reaction is indicated in some cases by fever. Approximately half the patients have died. The sexes were nearly equally represented. No age was exempt, but there were more patients in the fifth decade. The onset was more common (sixteen) in the summer. Various micro-organisms have been incriminated, generally streptococci and staphylococci. Dermatomyositis may be caused by various bacterial factors either as a direct invasion by way of the blood stream or as a toxic effect of bacterial products on the reacting tissues. Microscopic study of the earliest lesions of muscles indicates that the primary reaction may be manifested by the sarcoplasm rather than by interstitial cellular infiltration. As a rule the tempo of the onset signifies the rapidity of the course that will follow. Of thirty-eight patients followed, nineteen died in from four months to six years. Four patients have recovered completely. The dermatomyositis of none of these

was severe. In seven cases the condition has improved or is stationary, although accompanied by a variable amount of muscular incapacity. Of the eight patients whose condition has not improved, two have been observed too recently to permit comment on the course of the disease, three have suffered relapses and three have reported a slow, steady increase of weakness. Diagnostic problems are provided mostly by the early forms of the disease before distinctive muscular and cutaneous signs develop. Most difficult to distinguish from dermatomyositis are diffuse scleroderma in its edematous stage and sclerodema adultorum (Buschke). Other disorders to be differentiated are trichinosis, pellagra and lupus erythematosus. The course of dermatomyositis may at times simulate polyneuritis, myasthenia gravis, the myopathies, panniculitis, purulent embolic (septic) myositis, erysipelas, Addison's disease, acute rheumatic fever, periarteritis nodosa, postinfectious asthenias and functional states of exhaustion. Treatment of this disease of unknown cause is solely empirical and symptomatic. It includes the administration of vaccines, aminoacetic acid and sulfanilamide. At present a combination of artificial fever therapy, inhalations of oxygen and physical therapy appear most promising.

Archives of Neurology and Psychiatry, Chicago

43:1057-1298 (June) 1940

- *"Bulgarian Treatment" of Parkinson's Disease: Pharmacologic Aspects and Clinical Effects of Alkaloids of Belladonna Root. H. Vollmer, New York.—p. 1057.
Personality Changes Accompanying Cerebral Lesions: II. Rorschach Studies of Patients with Focal Epilepsy. M. R. Harrower-Erickson, Montreal.—p. 1081.
Neurohistopathologic Changes with Metrazol and Insulin Shock Therapy: Experimental Study on Cat. N. W. Winkelman and M. T. Moore, Philadelphia.—p. 1108.
Histologic Variations with Age in Apparently Normal Peripheral Nerve Trunks. Lillian Cottrell, Minneapolis.—p. 1138.
Cerebral Air Embolism and Vital Staining: Contribution to Experimental Study of Blood-Brain Barrier. S. M. Bouton Jr., Wrentham, Mass.—p. 1151.
Convulsions Associated with Tumors of Cerebellum: Clinical and Pathophysiologic Features. J. E. Webster and L. M. Weinberger, Philadelphia.—p. 1163.
Visuopsychic Apparatus and Accommodation Reflex. R. Y. Herren, Portland, Ore.—p. 1185.
Apparent Dedifferentiation of Nerve Cells of Human Brain as Result of Prolonged Starvation. W. Andrew, Dallas, Texas.—p. 1188.
Craniopharyngioma in Third Ventricle of Brain: Partial Surgical Removal and Pathologic Study. H. Zeitlin and E. Oldberg, Chicago.—p. 1195.
Sealing Specimens of Brain with Pliofilm: Practical and Inexpensive Way to Exhibit Specimens. L. W. Darrach, Northampton, Mass.—p. 1205.
Direct Psychotherapy of Children. M. Gitelson, Chicago.—p. 1208.

"Bulgarian Treatment" of Parkinsonism.—Vollmer tried the principal three alkaloids of belladonna root, hyoscyamine, scopolamine and atropine, in a synthetic compound in systematically varied and different combinations in the treatment of thirty patients with Parkinson's disease. The studies indicated that the range of greatest efficacy with the smallest possible dose was a combination of the three alkaloids in the following proportions: hyoscyamine from 75 to 95 per cent, atropine from 5 to 15 per cent and scopolamine from 1 to 5 per cent. An empirical combination consisting of hyoscyamine hydrobromide 90.2 per cent, atropine sulfate 7.4 per cent and scopolamine hydrobromide 2.4 per cent seemed particularly effective and was preferred by 90 per cent of the patients. This alkaloid compound was made up as an aqueous-alcoholic solution containing 3 mg. of total alkaloids per cubic centimeter and 66 per cent alcohol. Tablets of identical composition were also prepared, each containing 0.5 mg. of total alkaloids. One of these tablets corresponded quantitatively to four or five drops of the aqueous-alcoholic solution. This synthetic compound proved to be of at least the same efficacy as the most effective natural extracts of Bulgarian roots. On the basis of this definite clinical observation any obscure suppositions or mystic implications (nature healing) about the Bulgarian treatment can be dismissed. An average daily dose of from 2 to 3 mg. of this alkaloid compound was necessary to obtain an optimal clinical result. A pharmacodynamic synergism of the three alkaloids must be assumed. Even with this assumption, the effect on the central nervous

system in parkinsonism cannot be explained. Nevertheless a combination of these alkaloids brings about striking results. The treatment should be started with very small doses, which are gradually increased. All other medication must be discontinued. The required dose for each patient varies from one half to seven tablets three times a day but ranges on the average from one and one half to two tablets three times a day, or from 2.25 to 3 mg. of total alkaloids daily. Slight dizziness, dryness of the throat or sluggishness are occasionally described by the patients and are signs of overdosage. Not all symptoms of the disease respond to the drug simultaneously or to the same extent. General spirits and muscular rigidity are the first to respond. Parkinsonian patients are sensitive, good natured, trustful, thankful and cooperative and have a strong desire to get well. It is important to encourage them until obvious clinical improvement is obtained. Hopelessness and skepticism delay the objective improvement. Fifty-two patients were treated, thirty-four of whom had postencephalitic parkinsonism and eighteen non-encephalitic paralysis agitans. Fifty per cent of the post-encephalitic but only 17 per cent of the nonencephalitic patients were markedly improved. There was moderate improvement in a further 32 and 33 per cent of the two respective groups. Four patients who had chronic encephalitis became entirely free from symptoms. In nonencephalitic parkinsonism only partial relief can be expected. Nevertheless, even this limited improvement may turn a complete invalid into a person who can enjoy some degree of independence and take part in some activities. The majority of the improved patients were able to work. Treatment with the belladonna alkaloid compound is symptomatic and must be continued indefinitely. Supplementary psychotherapy is valuable.

Delaware State Medical Journal, Wilmington

12:73-136 (May) 1940

- Crime and Psychiatry. M. A. Tarumian, Farnhurst.—p. 73.
Endocrine Therapy in Mongolian Idiocy. C. W. Dunn, Philadelphia.—p. 78.
Need for More Physical Study of Mental Cases. P. F. Elfeld, Farnhurst.—p. 84.
Adrenal Neurocytoma. J. W. Ballard, Farnhurst.—p. 86.
Psychosis Following Secondary Anemia: Report of Two Cases. F. Paul, Farnhurst.—p. 89.
The General Practitioner and Psychiatry. H. W. Mikkelsen, Farnhurst.—p. 91.
Functional Psychosis and Brain Tumor. G. J. Gordon, Farnhurst.—p. 93.
Insufficiency in Adrenal Cortex. F. Freytag, Farnhurst.—p. 96.
Psychosis Associated with Psychopathic Constitution. M. Zimble, Farnhurst.—p. 99.
Preventive Psychiatry: Presentation of Two Cases from the Child Guidance Clinic to Illustrate Treatment Methods. M. L. Wadsworth, Farnhurst.—p. 103.
Surgical Aspects of Essential Hypertension. G. Bieringer, Farnhurst.—p. 108.
Importance of the Art Department for the Interpretation of Psychic States. F. Freyhan, Farnhurst.—p. 111.
Sulfanilamide—Local Application in Dentistry. W. H. Norris, J. A. Wiener and I. L. Yalisove.—p. 118.

Journal of Pharmacology & Exper. Therap., Baltimore

69:1-102 (May) 1940. Partial Index

- Studies of Actions of Methyl-Adrenalin; Methadren. J. W. Stutzman and O. S. Orth, Madison, Wis.—p. 1.
Toxicologic Studies on Cubé. H. B. Haag and Isabel Taliaferro, Richmond, Va.—p. 13.
Influence of Hydrogen Ion Concentration on Absorption of Alkaloids from Stomach. Janet Travell, New York.—p. 21.
Acetylation of Sulfanilamide and Sulfapyridine in Cat. W. Van Winkle Jr. and W. C. Cutting, San Francisco.—p. 40.
Comparison of Coronary Vasodilator Activity of Certain Alkyl Xanthines. G. V. LeRoy and J. H. Speer, Chicago.—p. 45.
Respiratory Alkalosis During Anesthesia: III. Hemoglobinemia Following Prolonged Hyperventilation. R. T. Stormont, M. H. Seevers, F. E. Shideman and T. J. Becker, Madison, Wis.—p. 68.
Therapeutics of Experimental Hypertension. A. Grollman, Baltimore; T. R. Harrison and J. R. Williams Jr., Nashville, Tenn.—p. 76.
Clinical Comparison of Picrotoxin, Metrazol and Coriamyrtin Used as Analeptics and as Convulsants. W. J. Bleckwenn, E. R. Hodgson and R. P. Herwick, Madison, Wis.—p. 81.
Comparative Therapeutic Activity of Sulfanilamide, Sulfapyridine and Diaminosulfone in Streptococcus Infections in Mice. E. K. Marshall Jr., J. T. Litchfield Jr. and H. J. White, Baltimore.—p. 89.

Journal of Urology, Baltimore

43:767-930 (June) 1940. Partial Index

- Hypernephroma in Polycystic Kidney: Review of Literature and Report of Case. M. M. Melicow and H. H. Gile, New York.—p. 767.
- *Staphylococcal Infections of Renal Cortex: Analysis of Five Additional Cases of Carbuncle and Six Additional Cases of Abscess. P. J. Kahle, M. M. Green and G. Tomskey, New Orleans.—p. 774.
- Some Aspects of Pathology of Pylonephritis. W. G. J. Putschar, Charleston, W. Va.—p. 793.
- Lymph Collectors from Ureters, Their Regional Nodes and Relations to Posterior Abdominal Lymph Channels. Alice E. Parker, Denver.—p. 811.
- Urethrography in Bulbo-Urethral Adenitis. M. L. Brodny and S. A. Robins, Boston.—p. 844.
- *Tumors of Testis: Study of Pathology of 142 Cases of Primary Neoplasms of Testis in Man. W. G. Gordon, Ann Arbor, Mich.—p. 851.
- Initial Priapism During Therapy with Testosterone Propionate in Eunuchoid Man. Rita S. Finkler, Newark, N. J.—p. 866.
- Male Infertility from Gynecologic Point of View. S. R. Meaker, Boston.—p. 871.
- Histaminase and Histamine Desensitization in Genito-Urinary Allergy. H. M. Johnson, San Antonio, Texas.—p. 891.
- Study of Bactericidal Activity of Sulfanilamide in Urine at Various Levels of Hydrogen Ion Concentration. J. R. Sickler, Rochester, Minn.—p. 906.

Staphylococcal Infections of Renal Cortex.—Kahle and his colleagues add five cases of renal carbuncle to the two reported in 1933 and also report six cases of renal cortical abscess. These eleven cases were encountered at Charity Hospital during a period of three years. In the authors' opinion the lesions of the renal cortex are not identical with renal carbuncle and do not, as some authors claim, represent separate stages of the same lesion. They may be single or multiple. Pathologically they differ in many respects. The distinction was particularly well marked in one case in which there was a carbuncle of the upper pole of the kidney and multiple discrete abscesses elsewhere in the renal cortex. The abscesses were widely separated from the carbuncle and from one another and presented none of the characteristics of the carbuncle. Both lesions are undoubtedly the result of blood borne infection, but the carbuncle, because of its wedge shape, probably arises from occlusion of an artery by septic embolus; later the infarction goes on to suppuration. The abscess is probably caused by bacteria which have lodged in a glomerulus without complete occlusion. Later central necrosis and abscess formation occur at this point. The origin of the renal infection is a primary focus. A history of a previous carbuncle, furuncle, paronychia, tonsillar infection, trauma or infection of a simple cut was elicited in eight of the eleven cases. From eight to twelve weeks elapsed before symptoms of cortical renal infection ensued. The carbuncle is separated from the cortex by a wall of thick fibrous tissue. The suppurating areas, which vary in size, may or may not connect with one another and the craters never contain large amounts of pus. The lesion is not fluctuant and is hard to the touch. The suppurating craters contain thick creamy or greenish pus. The base is somewhat raised above the surface of the kidney, and the overlying capsular tissue is thick and greatly infiltrated. The cortical abscess is round or oval. Fluctuation can be made out even when it is tense, and the characteristic induration of the carbuncle is lacking. When the lesion is close to the surface of the kidney, areas of dirty white or creamy hyperemia surround it. When the lesion ruptures or is incised and purulent contents are completely evacuated, the cavity is rather soft and smooth to the touch. Staphylococcus aureus was found in seven cases and Staphylococcus albus in three of the ten in which such study was made. Treatment is essentially surgical, but radical operation is not always necessary. A lower mortality usually follows nephrectomy, but excellent results can be achieved by conservative procedures in properly selected cases. Early diagnosis and prompt surgical intervention decrease the mortality and the post-operative morbidity. The time element is therefore an important factor in the final outcome.

Tumors of Testis.—Gordon analyzed the pathologic material of 142 primary neoplasms of the testis in an endeavor to interpret their pathogenesis. Special attention was given to the histopathology of the tumors and the presence of teratomatous structures. Any tumor was considered to be of teratomatous origin if tissues were demonstrated in it which could not conceivably have arisen from adult germinal epithelium or normal testicular supporting tissues by anaplastic or metaplastic changes.

Therefore such structures as striated muscle, cartilage, mucin-forming columnar epithelium or any malignant neoplasm derived from these, as a mucin-forming adenocarcinoma, were considered to be teratomatous in origin. Eighty of the 142 tumors were of teratomatous origin and in sixty-two this origin was not proved. The author states that the evidence favors the hypothesis that essentially all neoplasms of the testis are of teratomatous origin, with cellular overgrowth of one germ layer often producing homogeneous neoplasms which resemble germinal epithelium. Careful search will reveal teratomatous remains in many characteristic neoplasms of this type, which cannot be distinguished microscopically from those in which teratomatous elements cannot be found. The occurrence of teratomatous elements exceeds the expected incidence of coexistence of two primary neoplasms in the same organ, and therefore the teratoma should be accepted as significant of the pathogenesis. No transition stages were found between normal germinal epithelium and embryonal carcinoma (seminoma) or adenocarcinoma. The study offers no additional evidence as to the origin of teratomas in the testis.

Kansas Medical Society Journal, Topeka

41:189-232 (May) 1940

- Rose Operation: Repair of Trigonal Muscle (Incontinence in the Female). F. W. Matassarini, Wichita.—p. 189.
- Artificial Fever Therapy. L. F. Glaser, Kansas City.—p. 192.
- Clinical Illustration of Acid-Base Imbalance. F. C. Neff, Kansas City, Mo.—p. 196.
- Ten Year Statistical Study of Cesarean Section in Sedgwick County. R. H. Maxwell, Wichita.—p. 199.

Laryngoscope, St. Louis

50:373-502 (May) 1940

- Progressive Deafness, Otosclerosis and Closely Related Subjects: Abstract of Available Literature Published During the Year 1939. J. A. Babbitt, Philadelphia.—p. 385.
- Stenosis of Larynx Due to Paralysis of Vocal Cords: Treatment by Submucous Resection of Vocal Cords: Report of Operated Cases. J. H. Maxwell, Ann Arbor, Mich.—p. 452.
- Pathologic Conditions of Esophagus. L. H. Clerf, Philadelphia.—p. 463.
- Hoarseness: New Classification and Brief Report of Four Interesting Cases. D. I. Frank, New York.—p. 472.
- Otorhinologic Sequelae of Swimming: Analysis of Present Concepts: New Method of Prevention. D. Mezz, Brooklyn.—p. 479.

Medicine, Baltimore

19:161-328 (May) 1940

- Uric Acid Content in Blood and Urine in Health and Disease. K. Brøchner-Mortensen, Copenhagen, Denmark.—p. 161.
- Acute Hemolytic Anemia (Acquired Hemolytic Icterus, Acute Type). W. Dameshek and S. O. Schwartz, Boston.—p. 231.

New England Journal of Medicine, Boston

222:901-942 (May 30) 1940

- Immunity to Virus Diseases: Some Theoretical and Practical Considerations. E. W. Goodpasture, Nashville, Tenn.—p. 901.
- Hydronephrosis: Standardization of Surgical Treatment. T. E. Gibson, San Francisco.—p. 910.
- Appendices Epiploicae. G. A. Moore, Brockton, Mass.—p. 919.

222:943-984 (June 6) 1940

- Blood Phosphorus Studies in Rheumatic Fever. N. Epstein and F. C. McDonald, Boston.—p. 943.
- End Results of Use of Large Doses of Amphetamine Sulfate over Prolonged Periods. W. Bloomberg, Boston.—p. 946.
- *Prevention and Management of Pain Following Cholecystectomy. J. M. McGowan and F. F. Henderson, Boston.—p. 948.
- Importance of Investigating Cause of Renal Pain. H. G. Nichols, Haverhill, Mass.—p. 954.

Pain Following Cholecystectomy.—McGowan and Henderson point out that, after surgical removal of the gallbladder, pain and discomfort often return and are as severe as they were before the operation. Biliary colic following cholecystectomy is due to obstruction of the common duct, preventing the flow of bile into the duodenum. Obstruction of the common duct may be due to stone, stricture, edema or spasm. The back pressure results in pain. Common duct pressure of 70 mm. of water produces pain in some individuals, while 500 mm. may be withstood by others with impunity. Prolonged T-tube drainage allows the common duct to resist greater pressures. Glycerol trinitrate relaxes duodenal spasm and tends to lower

the intrabiliary pressure. The authors describe methods for studying the patency of the papilla of Vater and the condition of the bile ducts. They show that biliary dyskinesia and many symptoms of cholecystitis are relieved by a course of treatment consisting of the daily use of glyceryl trinitrate to relax duodenal spasm.

New Orleans Medical and Surgical Journal

92:665-730 (June) 1940

- Angina Pectoris and Coronary Thrombosis. W. R. Wirth, New Orleans.—p. 671.
Plasma Proteins: Methods of Determination and Clinical Significance. H. H. Beard, New Orleans.—p. 678.
Effects of War on Mental Health. C. S. Holbrook, New Orleans.—p. 681.
Acute Epidural Abscess of Spinal Canal. D. H. Echols, New Orleans.—p. 682.
Acute Spontaneous Cerebral Vascular Accidents in Adults: Review. L. K. Levy, New Orleans.—p. 683.
Vincent's Cervicitis. J. P. Quindlen and L. Tauhenhaus, Brooklyn.—p. 692.
Treatment of Tularemia with Thiazole Derivatives of Sulfanilamide. J. O. Weillhaeher Jr. and Emma S. Moss, New Orleans.—p. 694.
Modern Medical Illustrating. T. Jones, Chicago.—p. 697.
Francesco Antommarchi (1780-1838). R. Glenk, New Orleans.—p. 701.

New York State Journal of Medicine, New York

40:837-908 (June 1) 1940

- *Ambulatory Insulin Treatment of Mental Disorders. P. Polatin, H. Spotnitz and B. Wiesel, New York.—p. 843.
Acute Putrid Abscess of Lung—Surgical Disease. H. Neuhof and A. S. W. Touroff, New York.—p. 849.
Use of Tubed Pedicle Flaps for Study of Wound Healing in Human Skin. L. E. Sutton, Syracuse.—p. 852.
Pulmonary Apical Tumefaction Simulating Bursitis: Necessity for Routine Chest Examination in Patients with Shoulder Pain. L. Nathanson, Brooklyn.—p. 860.
Modern Concepts of Mental Illnesses. G. S. Sprague, White Plains.—p. 865.
Infected Renal Cyst. B. Davidson, Brooklyn.—p. 875.
Rapid Method for Checking Position of Tube During Gastric Gavage. E. Messinger, Brooklyn.—p. 882.
A New Skin Thermometer. S. S. Samuels, New York.—p. 884.
Let Us Wassermannize the Expectant Father. M. Berlind, Brooklyn.—p. 885.

Ambulatory Insulin Treatment of Mental Disorders.—Polatin and his associates gave small doses of insulin hypodermically to twenty-two unselected patients with mental disease of functional or organic type. The functional group included eighteen patients with schizophrenia, manic-depressive psychosis or psychoneurosis. The organic group consisted of four patients with definite cerebral lesions associated with hypertensive cardiovascular disease, cerebral arteriosclerosis, an organic syndrome following removal of a pineal tumor or organic brain disease of an undetermined type. Patients were given one hypodermic injection of insulin daily at 5 a. m. and had the usual hospital breakfast at 8 o'clock. The initial dose was 5 units. This was increased daily by 5 units until a mild hypoglycemic shock, characterized by usual symptoms of weakness, giddiness, tachycardia, vasomotor alterations, excessive perspiration and some drowsiness, was obtained. Usually the hypoglycemic symptoms began about two hours after the injection and gradually increased in severity. Hypoglycemia was permitted for from fifteen to forty-five minutes. The 40 units of insulin in one dose was sufficient to produce the desired effect. The hypoglycemic state was usually terminated with breakfast. During hypoglycemia the patients were up and about. The mild hypoglycemic symptoms did not prevent the patients from feeding themselves at breakfast without any assistance. The twenty-two patients were treated over a period ranging from one week to eighteen months. Transitory alterations in the mental status of the patients were observed during the daily treatment period and in some instances continued for a few hours thereafter. Agitated and excited patients were quieted, states of confusion were cleared, and dulness and apathy gave way to increased alertness. Such beneficial changes gradually persisted for longer periods after each treatment until definite clinical improvement was maintained. Even the four unimproved patients were influenced sufficiently by the insulin treatment so that nursing and feeding problems were simplified. All patients gained weight with an accompanying increase in appetite. One patient recovered, twelve

were much improved and five were slightly improved. The much improved patients were able, despite residual symptoms, to adjust themselves socially at a level paralleling their pre-morbid behavior. The slightly improved patients showed a definitely increased ability to adjust themselves to the hospital routine but did not reach their pre-morbid behavior level because of residual symptoms. No coma, allergic manifestations, convulsions or observable injuries occurred during treatment.

Northwest Medicine, Seattle

39:199-234 (June) 1940

- Hypertension. N. C. Gilbert, Chicago.—p. 202.
Allergic Skin Disorders: Practical Approach to Their Management. F. Perlman, Portland, Ore.—p. 205.
Vitamin Therapy in Dermatologic Practice. T. S. Saunders, Portland, Ore.—p. 209.
Treatment of Certain Allergic Skin Conditions with Histaminase. A. R. Altose, Seattle.—p. 212.
Histaminase in Treatment of Peptic Ulcer. P. O'Hollaren, Seattle.—p. 216.
Calcification of Pericardium: Edema of Head and Neck a Symptom. C. I. Drummond, Medford, Ore.—p. 217.
Bilateral Anterior Lenticonus, with Congenital Discoid Punctate Cataracts. C. F. Harris, Klamath Falls, Ore.—p. 219.
Ideal Vaccination Technic. H. M. Page, Portland, Ore.—p. 220.
Pneumococcal Meningitis Treated Successfully: Case Report. S. Vukov, Seattle.—p. 221.

Ohio State Medical Journal, Columbus

36:585-712 (June) 1940

- Anxiety Neurosis. H. Evans and G. T. Harding, Columbus.—p. 601.
Cancer of Body of Uterus. T. H. George, Cleveland.—p. 606.
Exercise in Tuberculosis: Plea for Conservatism. W. J. Habeeb, Mount Vernon.—p. 609.
Volvulus: Case Report. J. J. Marek, Cleveland.—p. 611.
Early Diagnosis of Syphilitic Aortitis. J. W. Martin, Cleveland.—p. 612.
Cleveland City Hospital Observations on Sources of Infection in Syphilis. H. E. Freeman, Cleveland.—p. 616.
Compression of Upper Ureter by Metastatic Embryonal Carcinoma of Perireticular Lymph Node, Primary in Testis. W. Rosenberg, Cleveland.—p. 620.
Selection and Management of Anesthesia for Upper Abdominal Surgery. J. D. Spaid, Dayton.—p. 624.
Treatment of Cancer of Nose and Throat. E. King, Cincinnati.—p. 627.
Mucocele of Appendix. C. B. Elliott, Painesville.—p. 629.
Rheumatic Fever in Children. R. A. Lyon, Cincinnati.—p. 631.
Chronic Acetanilid Poisoning: Report of Case. N. Michael, Columbus.—p. 632.

Pennsylvania Medical Journal, Harrisburg

43:1249-1376 (June) 1940

- The Neurogenic Bladder. R. M. Neshit and W. G. Gordon, Ann Arbor, Mich.—p. 1261.
Psychotic Manifestations in Physical Disease and in Reaction to Drug Therapy. A. P. Noyes, Norristown.—p. 1269.
Safety Measures in Intracapsular Cataract Extraction. H. E. Thorpe, Pittsburgh.—p. 1280.
Antiseptized Hose as an Aid in Pedal Acromyocosis. S. S. Greenbaum and J. W. E. Harrison, Philadelphia.—p. 1289.
Amaurotic Family Idiocy. G. J. Feldstein, Pittsburgh.—p. 1296.
Prescribing a Hearing Aid. K. M. Day, Pittsburgh.—p. 1299.
Empyema in Children. E. W. Meredith, Pittsburgh.—p. 1303.
*Treatment of Empyema with Hydroxyethylapocupreine Dihydrochloride. Maud L. Menten and R. R. MacDonald, Pittsburgh.—p. 1305.

Hydroxyethylapocupreine Dihydrochloride for Empyema.—Menten and MacDonald treated twenty-five children suffering from empyema with hydroxyethylapocupreine dihydrochloride. From 25 to 150 cc. of the drug, preferably dissolved in a slightly alkaline solution in a concentration of 1 per cent, was injected and left in the empyema cavity after a fairly complete evacuation of the pus was complemented by irrigation with the dissolved drug. Irrigation and instillation were repeated every third day. Usually after the second or third treatment the pus became sterile, the temperature returned to normal and the appetite improved. As the amount of pus progressively diminished, the temperature gradually approached normal. With evacuation and irrigation alone there was a temporary fall in temperature followed by prompt refilling of the empyema cavity with pus, which always gave a positive culture for pneumococcus. If the condition had existed for three or four weeks it usually did not respond to treatment as readily as when the disease was of shorter duration. The number of taps, combined with instillation of the drug, varied from three to twelve and the amount of drug used ranged from 195 to 1,200 cc. The

time required for cure varied from eleven to thirty-seven days, with an average of twenty-six days. Of the twenty-five children who received the closed treatment, nineteen were adequately and six were only partially treated. These six children were subsequently transferred to the surgical service for rib section. Fourteen of the nineteen patients responded favorably to treatment and were discharged completely cured. Three of the remaining five patients who failed to show favorable results had complicating pathologic disorders: an additional streptococcal infection, a recurrent pneumonia and an obscure abdominal condition. The drug therapy was ineffectual for the other two. The fourteen operated on (eight previously treated with the drug, two of the ineffectually and the six partially treated patients) were discharged from the hospital on an average of twenty-seven days after operation, returning to the dispensary for dressings. The average time required for the eradication of the empyema was approximately the same for the two. Hydroxyethylapocupreine dihydrochloride could undoubtedly be made more effective by the use of oxygen instillation to control pressures during evacuation of pus and by treating patients before the fibrin layers become too thick. More concentrated solutions of the drug for instillation and better technical removal of pus, as with Miller or Robinson pneumothorax needles, might shorten the time of treatment. Blood transfusions might be helpful in building up the child's resistance. The use of the drug is limited to pneumococcal empyemas and to cases in which no inaccessible encysted pus is present.

Public Health Reports, Washington, D. C.

55:915-954 (May 24) 1940

Determination of V Factor in Urine and Tissues of Normal Dogs and of Dogs with Blacktongue by Use of *Haemophilus Parainfluenzae*. Margaret Pittman and H. F. Fraser.—p. 915.
Two New Species of Argasidae (Acarina: Ixodoidea). R. A. Cooley and G. M. Kohls.—p. 925.

55:955-1002 (May 31) 1940

Prevalence of Poliomyelitis in the United States in 1939. C. C. Dauer.—p. 955.
The Course of Disabling Morbidity Among Industrial Workers, 1921-1938. W. M. Gafar.—p. 962.
Studies of Sewage Purification: XIII. Biology of *Sphaerotilus Natans* Kutzing in Relation to Bulking of Activated Sludge. J. B. Lackey and Elsie Wattie.—p. 975.

Review of Gastroenterology, New York

7:203-304 (May-June) 1940

Splanchnoptosis as Potential Anatomic Path to Gastric and Duodenal Ulcer. Agnes C. Vietor, Boston.—p. 203.
Visceroptosis. M. G. Spiesman, Chicago.—p. 218.
Comparative Study of Methods Utilized to Determine Presence of Ulceration in Gastrointestinal Tract, with Special Note on the Woldman Phenolphthalein Test. A. L. Levin and M. Shushan, New Orleans.—p. 235.
Why Does Gastro-Enterostomy Fail? V. G. Burden, Philadelphia.—p. 242.
Tuberculosis of Retroperitoneal Lymph Nodes with Long Clinical Course of Obscure Fever. H. L. Rakov and J. S. Taylor, Kingston, N. Y.—p. 246.
Lymphosarcoma of Ileocecal Valve. R. Schaaf and M. Kraemer, Newark, N. J.—p. 248.
Micro Method for Quantitative Determination of Ammonia in Feces Without Distillation. F. Rappaport and L. Lissner, Manila, P. I.—p. 251.
Medical Management of Cholelithiasis. J. Friedenwald, S. Morrison and M. Feldman, Baltimore.—p. 256.
Evaluation of Some Liver Function Tests in Intrahepatic and Extrahepatic Jaundice. R. Upham and N. W. Chaikin, New York.—p. 263.
New Physiologic Test for Liver Function: Preliminary Report. L. M. Morrison and W. A. Swalm, Philadelphia.—p. 269.
Toxic Hepatitis. A. Levitt and D. S. Levy, Buffalo.—p. 275.
Coexistence of Gaucher's Disease and Cholelithiasis. E. Rosenthal, Budapest, Hungary.—p. 278.

Rocky Mountain Medical Journal, Denver

37:393-472 (June) 1940

Occupational Dermatoses. H. R. Foerster, Milwaukee.—p. 410.
Coronary Occlusion: Its Differential Diagnosis. E. S. Kilgore, San Francisco.—p. 419.
Roentgen Therapy in Inflammatory Diseases. J. S. Bouslog, Denver.—p. 422.
Use and Misuse of Iodine in Prevention and Treatment of Goiter. E. W. Barber, Denver.—p. 427.
Management of Hyperthyroidism. E. Snow, Salt Lake City.—p. 430.
Postoperative Tetany. G. G. Richards, Salt Lake City.—p. 436.
Amputations to Obtain Greatest Functional Value. C. C. Haddan, Denver.—p. 440.

Southern Surgeon, Atlanta, Ga.

9:381-458 (June) 1940

Cystoscopic Photography: Preliminary Report. E. G. Ballenger, H. P. McDonald and R. C. Coleman Jr., Atlanta, Ga.—p. 381.
Sex Endocrinology and Pelvic Surgery. R. A. Ross, Durham, N. C.—p. 387.
Suprapubic Prostatectomy with Use of Original Combination Hemostatic and Drainage Tube. L. P. Thackston, Orangeburg, S. C.—p. 403.
Postoperative Pulmonary Complications. J. B. Lukins, Louisville, Ky.—p. 411.
Significant Factors in Prognosis and Mortality of Perforated Peptic Ulcer. M. DeBakey and C. B. Odom, New Orleans.—p. 425.
Melanomas: Clinical Discussion. Q. B. Lee and J. R. Mast, Wichita Falls, Texas.—p. 437.
Interpretation of Diarrheas Encountered in Proctologic Practice. M. S. Kleckner, Allentown, Pa.—p. 442.

Surgery, Gynecology and Obstetrics, Chicago

70:987-1124 (June) 1940

*Effect of Zinc Peroxide Treatment on Ulcers Due to Micro-Aerophilic Hemolytic Streptococcus. T. A. Shallow, K. E. Fry and E. J. Pulaski, Philadelphia.—p. 987.
Clinical Use of Gonadotropic Hormone from Pregnant Mare Serum. C. P. Huher and M. E. Davis, Chicago.—p. 996.
Comparison of Prothrombin Levels of Maternal and Cord Blood at Delivery. R. F. Norris and A. Rush, Philadelphia.—p. 1006.
*Lung Abscess: Analysis of the Massachusetts General Hospital Cases from 1933 Through 1937. R. H. Sweet, Boston.—p. 1011.
*Acute Cholecystitis: Review of 320 Cases. L. S. Fallis and R. D. McClure, Detroit.—p. 1022.
Scoliosis: Its Experimental Production and Growth Correction; Growth and Fusion of Vertebral Bodies. J. D. Biscard and M. M. Musselman, Omaha.—p. 1029.
Cancer of Thyroid. W. L. Watson and J. L. Pool, New York.—p. 1037.
Splenectomy. A. O. Singleton, Galveston, Texas.—p. 1051.
Repair of Inguinal Hernia: Standardized Technic. J. J. Stein and P. F. Brown, Hines, Ill.—p. 1054.
Peripheral Vascular Disease: Critical Survey of Its Conservative and Radical Treatment. A. Ochsner and M. DeBakey, New Orleans.—p. 1058.
Treatment of Extensive Wounds: Notes on Six Cases in Which Injuries Were Caused by Circular Saw. J. H. Powers, Cooperstown, N. Y.—p. 1073.
Preserved and Fresh Homotransplants of Cartilage. J. B. Brown, St. Louis.—p. 1079.
Carcinoma of Body of Uterus: Experience of the Mayo Clinic for Twenty-Four Years. J. C. Masson and R. O. Gregg, Rochester, Minn.—p. 1083.
Technic of Combined Division, Ligation and Injection of Incompetent Great Saphenous Vein. L. K. Stalker and W. W. Heyerdale, Rochester, Minn.—p. 1094.
Simple Nonspecific Ulcer of Jejunum-Ileum. D. R. Robinson and W. D. Wise, Baltimore.—p. 1097.
Ovarian Lesions Simulating Appendicitis. C. C. Guy and A. J. Rotondi, Chicago.—p. 1100.

Zinc Peroxide Treatment for Streptococcal Ulcers.

—Shallow and his colleagues report six cases of chronic undermining ulcers due to the micro-aerophilic hemolytic streptococcus, stress the importance of early diagnosis, urge that anaerobic as well as aerobic cultures be requested as a routine in all cases with frank suppuration which fail to respond to ordinary measures and reaffirm the favorable influence of zinc peroxide cream dressings on the course of the infection. These infections went along for indefinite periods (up to two and one half years) unrecognized as to etiology. The physicians who first saw the patients believed that they were dealing with ordinary slow healing wounds. The patients were hospitalized only after trial and failure of the customary methods of treatment. The diagnoses were in many cases revised with lack of success with one treatment and substitution of another. Possibly because of the infrequent report of such cases in the literature, chronic undermining, burrowing ulcer was not mentioned early as a possible diagnosis. The fact that these ulcers may improve temporarily under various treatments is misleading and may tend to delay the true diagnosis. Their diagnosis is difficult unless anaerobic as well as aerobic bacteriologic studies are carried out. The invasive organism grows much better anaerobically than aerobically, at least early in the disease. It may be missed on the aerobic plates, especially in the presence of rapidly growing secondary contaminants. The same holds true in long standing infections in which the colonies of hemolytic streptococci growing on the aerobic plates are few in number. Therefore material from the ulcers should be planted immediately on mediums under anaerobic as well as aerobic conditions. It is practicable to advise the laboratory to search for the micro-

aerophilic hemolytic streptococcus. One of the authors' cases is representative of the way these infections may continue for months or years with extensive destruction of tissues before the true cause is recognized. The disease began as a trivial abrasion and spread with involvement of the surrounding skin and subcutaneous tissues until there was extensive destruction. The failure to heal was attributed to the presence of syphilis. When syphilitic therapy in conjunction with various antiseptics failed to effect a cure, a diagnosis of stasis ulcer was made. The regressions were explained on the basis of secondary infection. Each time that the acute infection subsided the patient was discharged (six times) from the hospital and was treated as an ambulatory case. It was not until the fifth admission that further possibilities were looked into, and this after two amputations and several débridements had already been made. An earlier diagnosis might have been made had there been (1) true appreciation of the clinical manifestations of this infection, (2) consideration of chronic burrowing indolent ulcer in the list of differential diagnoses and (3) adequate and complete bacteriologic studies. Earlier institution of zinc peroxide treatment might have saved this man's limb. Failure to obtain permanent improvement with ordinary measures should serve as the most forceful argument for the urgent need of early diagnosis. Freshly prepared potent zinc peroxide cream when applied to all affected parts of such a wound and protected against drying is dramatic. Within a few days the exudation ceases, granulations start filling in, the undermining becomes less and the wound takes on a healthy appearance. For successful treatment the zinc peroxide cream must reach all parts of the wound and the preparation must be potent.

Lung Abscess.—Sweet offers the following suggestions, based on a study of 125 cases of lung abscess, for improving the therapeutic results: 1. Patients should not be allowed to go without operation longer than four months from the onset of disease. 2. Patients with abscesses who do not show definite regressive changes should be operated on within six to eight weeks after onset; often as soon as they are seen and the diagnosis is confirmed. 3. The interval between the two stages of the operation should not exceed four or five days; in the desperately sick patients, not more than twenty-four or forty-eight hours. 4. The abscesses of the upper lobe which are not too acute should be subjected to primary lobectomy in preference to drainage. 5. Certain abscesses should be drained as a preliminary procedure with the idea of performing a lobectomy at a later date. 6. Redrainage should be abandoned. Patients whose wounds remain unhealed after primary drainage will do better if subjected to lobectomy. The opening of secondary cavities not reached at the first operation is not classified as redrainage. 7. All patients with lung abscess should have the benefit of the combined judgment of the internist, the bronchoscopist, the thoracic surgeon and the roentgenologist. Improved results will probably ensue if the bacteriology and the related problems of immunology in these cases are understood better.

Acute Cholecystitis.—According to Fallis and McClure, the mortality in 320 consecutive operations for acute cholecystitis performed at the Henry Ford Hospital was 5.3 per cent. The maximal preoperative temperature is of some prognostic value. The death rate of patients whose preoperative temperature was above 102 F. was three times that of those whose temperature remained below 102 F. Preoperative pulmonary disease increased the risk of operation three times, and cardiac disease doubled it. The lowest mortality rate was obtained in cases in which operation was delayed for at least seventy-two hours from the onset of acute symptoms. It appears best to delay operation until the fluid balance is restored, the glycogen content of the liver is augmented and an estimate of liver function is made. The highest mortality rate was in the gangrenous cases. Gallstones were present in 90.9 per cent of the patients. A postoperative temperature of above 103 F. is of considerable prognostic value, for the mortality among such patients was 28 per cent. Less than 15 per cent of patients were discharged by the seventeenth postoperative day and more than 20 per cent remained in the hospital longer than thirty days. The short duration of life in the fatal cases—more than 80 per cent of the deaths occurred before the fifth postoperative day—suggests that hepatic insufficiency might be a factor in the mortality.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Children's Diseases, London

37:89-152 (April-June) 1940

- Erythroblastic Anemia. F. R. B. Atkinson.—p. 89.
- Dyschondroplasia (Ollier) of Upper Limb with Other Developmental Abnormalities. T. Anwyl-Davies and F. P. Weber.—p. 110.
- Encephalitis Complicating Whooping Cough with Subsequent Development of Epilepsy. C. Worster-Drought.—p. 115.
- Hydrops Foetalis: Case. J. V. O'Sullivan and J. R. Gilmour.—p. 119.

British Medical Journal, London

1:839-878 (May 25) 1940

- *Effect of Intrapartum and Neonatal Administration of Synthetic Vitamin K Analogues on Newborn. A. I. S. Maepherson, E. McCallum and W. F. T. Haultain.—p. 839.
- Perforated Jejunal Ulcer Following Partial Gastrectomy. W. A. Law.—p. 844.
- Use of Thiersch Skin Graft. B. K. Rank.—p. 846.
- Barbiturate (Soneryl) Poisoning: Account of Case Showing Value of Picrotoxin in Treatment. G. M. Slot.—p. 849.
- Tuberculosis: Case. T. F. Miles and M. Curwen.—p. 850.

Intrapartum and Neonatal Synthetic Vitamin K Administration.—Macpherson and his associates estimated the prothrombin index in fifty-four infants during the first week of life. The principal feature was the extreme variation in the prothrombin index between different individuals on the same day and in the same case on different days. An appreciable decrease from the cord estimation was often demonstrated within twenty-four hours and this fall continued, reaching its lowest value from thirty-six to eighty-four hours post partum. About the fifth day post partum the prothrombin level rose sharply and became stabilized at about 75 per cent. It gradually rose over a period of months. A vitamin K analogue was given in the early neonatal period to thirty-six babies. The administration of 2-methyl-1:4-naphthoquinone and diacetyl-2-methyl-1:4-naphthohydroquinone to twenty infants within twenty-four hours of birth raised the prothrombin index to from 80 to 90 per cent and stabilized it at that level during the first few days of life. This effect was independent of the cord prothrombin index, of the antenatal condition, of prematurity and of the type and duration of labor. The quinone given orally appeared to be less potent than quinol diacetate. The quinol diacetate corresponded closely in activity to the quinone parenterally. There was no difference in the effects produced by the injection of 2.5 mg. and 5 mg. of the quinone. The unusually rapid action of 2-methyl-1:4-naphthoquinone intramuscularly is confirmed by the effects in five cases. In one case an increase from 44 per cent to 63 per cent was noticed in 100 minutes, and in another from 50 per cent to 85 per cent in 150 minutes. Thirty-one mothers were given a vitamin K analogue ante partum. The effect on the prothrombin index of the infant during the first week of life was qualitatively identical with that obtained by giving the same substances directly to the baby during the first twenty-four hours of life. There is no advantage in giving more than 50 mg. by mouth to mothers. The maximal effect will be obtained in the newborn if an adequate dose is given to the mother between twelve and four hours before delivery. The contents of the intestine are sterile in the newborn. Therefore enough vitamin K cannot be absorbed until bacterial invasion of the bowel occurs. Breast feeding or the use of unsterilized breast milk on the first day should assist this synthesis by supplying numerous harmless bacteria, but this does not afford any protection against the fall in plasma prothrombin. Adequate administration of vitamin K analogue to the mother before delivery appears to be the most rational method of treating prothrombin deficiency in the newborn and its administration may become as routine as the use of vitamins A and D earlier in pregnancy. Its administration either to the mother before delivery or to the newborn would appear to be especially indicated (1) in cases of maternal toxemia, (2) in premature labor, (3) in difficult or instrumental delivery, (4) when breast feeding is not possible, (5) when any cerebral symptoms develop during the first few days of life, (6) in cases of hemorrhagic diathesis, ieterus gravis neonatorum and anemia and (7) when an operation is necessary on the newborn.

Medical Journal of Australia, Sydney

1:573-608 (April 27) 1940

*Antidiuretic Substance in Urine in Relation to Normal and Toxemic Pregnancy. Vera I. Krieger and T. B. Kilvington.—p. 575.
Recent Advances in Pathology of Blood Transfusion. N. M. Gutteridge.—p. 585.

1:609-650 (May 4) 1940

Pathology in Practice. K. Inglis.—p. 609.
Atelectasis and Pulmonary Tuberculosis. C. Harvey and B. White.—p. 613.
Australian Medical Work in Korea. C. I. McLaren.—p. 624.

Antidiuretic Substance in Urine in Pregnancy.—Krieger and Kilvington examined the urine of ten nonpregnant women, sixteen normal pregnant women, fourteen pregnant women with toxemia and eighteen with eclampsia for the presence of an antidiuretic substance. They describe their method for the preparation of the urinary extracts. Standard volumes of 100 cc. of urine, or protein-free filtrate from urine containing albumin, dialysed and concentrated to 10 cc., were used. The biologic assay of the urine preparations was done according to Burn's method for determining the antidiuretic potency of pituitary extracts. In this method, inhibition of water diuresis can be detected by the comparison of the urinary excretion of four mature male rats injected with preparations from the patient's urine with that of four control rats. Most workers have calculated the magnitude of the antidiuretic activity by measuring the difference in the times required for the volume of urine excreted by the rats injected with urine concentrates to equal half that of the water ingested and for the corresponding volume of urine to be excreted by the control rats. By this method only the time factor is taken into account. The authors emphasize that another method of assessing the antidiuretic potency of a urine concentrate is to determine its total effect by measuring the differences in the areas subtended by the graphs obtained when the total volumes of urine excreted by the control rats and by the treated rats are plotted against the time. In the present investigation both methods were used. The authors found that the method of the measurement of differences in areas shows delayed as well as immediate inhibitory effects and therefore is a more reliable means of estimating antidiuretic activity. Summarizing their results the authors state that a pituitary-like substance inhibiting water diuresis was found in small amounts in concentrates of the urine of some nonpregnant women and frequently in larger amounts in concentrates of the urine of normal pregnant women. Preparations from urine obtained from preeclamptic and eclamptic patients frequently contained large amounts of this antidiuretic hormone. The maximum concentration was observed at the height of toxemia, when albuminuria, oliguria, edema and raised blood pressure were present. With concentrates of 100 cc. samples from successive specimens of urine of patients suffering from eclampsia and preeclampsia, a sharp decrease in antidiuretic potency followed the maximum value and was accompanied by a decrease in edema and an increase in urinary excretion.

1:681-712 (May 18) 1940

Abdominal Pain and Integration of Patient. V. J. Kinsella.—p. 681.
*Modern Clinical Methods to Combat Whooping Cough Infection. S. W. Williams.—p. 690.
Trichomonas Vaginalis Vaginitis and Monilial Vaginitis: Their Diagnosis and Treatment. R. F. Matters.—p. 693.

Methods for Combating Whooping Cough.—Williams points out that of 144 ambulatory patients suffering from mild whooping cough, diagnosed on clinical evidence, 115 (80 per cent) gave positive reactions to cutaneous tests when first tested. Of the twenty-nine children who did not react to the first test, eleven gave a positive response on being retested three weeks later. The other eighteen children did not attend for a second test. These observations suggest that response to the test becomes positive during the progress of the disease. Twelve hospitalized children suffering from severe attacks for from four to thirteen weeks gave no reactions. An opportunity did not arise of testing these children during or after convalescence. Probably the reaction would have become positive. Twenty-nine of eighty-one children attending the Children's

Hospital for treatment for diseases other than pertussis had, according to the mothers, a history of whooping cough; ten gave positive reactions to cutaneous tests and nineteen did not. Of fifty-two children whose mothers stated that they had not had whooping cough, forty-seven gave no reaction and five gave positive reactions. There is a statistically significant correlation between a history of clinical whooping cough and a positive response to the cutaneous test. However, the correlation is not absolute. The five children may have suffered from a mild undiagnosed attack of whooping cough. Such attacks undoubtedly occur and can be diagnosed only by bacteriologic methods. Some or all of the nineteen children with histories of whooping cough who did not react to the cutaneous test may not have had whooping cough or the mother's statement may not have been completely reliable. On the other hand, it is not unlikely that the response to the test may change from "positive" to "negative" in a proportion of children within a few months or years after recovery. In the present state of knowledge it is probably safest to immunize all children who have not had whooping cough. By gradually increasing the initial and subsequent dosages of phase I vaccine in different groups of infants the author found it possible to give an initial dose of 7,500 million organisms and four subsequent injections of 20,000 million at weekly intervals. The injection was made into the deltoid muscle and the doses, except the first, were divided, 1 cc. of vaccine being injected into each arm. In about 10 per cent of 250 children the reactions were anorexia, fever (101 F.) and a tender erythematous area at the site of injection. About 30 per cent of infants were given two final doses of 30,000 million organisms to replace three injections of 20,000 each without severe reaction. Whether these 250 infants have been protected against whooping cough cannot be answered yet, as there has been no epidemic in Melbourne. Recent work shows that at least 80 per cent of infants immunized with phase I vaccine are protected against the disease. How long the immunity lasts and whether it is advisable to give a further dose of vaccine one year after the first injections are points still under debate. Until a method of testing a child's immunity, comparable perhaps with the Schick test for diphtheria is had, the control of dosage in whooping cough will be difficult. A ready source of possible antibody for passive immunization is parent's blood; 15 cc. of such blood is injected into each buttock. It is a somewhat painful procedure for the child, but the injected blood is apparently absorbed in twelve hours and no untoward reactions occur. Of fifteen infants treated thus the disease was mild in thirteen and severe in two. A comparison with forty-two controls shows twenty mild cases, eighteen severe and four cases of bronchopneumonia. An early diagnosis is essential for successfully lessening the effect of the disease. A positive cough-plate finding and the presence of a whoop are the only certain means of diagnosis. The former method is the only available one in the early stage of the disease.

Quarterly Journal of Medicine, Oxford

9:129-192 (April) 1940

Nitrogen and Chloride Metabolism in Gastrointestinal Hemorrhage. D. Black and A. Leese.—p. 129.
*Galactose Tolerance as Test of Liver Function. N. F. MacLagan.—p. 151.
*New Observations on Etiology and Prognosis of Achrestic Anemia. M. C. G. Israëls and J. F. Wilkinson.—p. 163.
A leukemic Leukemia. M. Hynes.—p. 177.

Galactose Tolerance as Test of Hepatic Function.—MacLagan determined the hepatic function by the galactose tolerance test of fifty normal persons (twenty healthy male medical students and thirty outpatients suffering from various diseases unconnected with the liver, thyroid or gastrointestinal tract), six cases of diabetes mellitus, ten of toxic jaundice, six of obstructive jaundice and twelve of exophthalmic goiter. The students gave a slightly lower reading than the normal controls. However, the difference was hardly great enough to be of clinical importance. All the toxic and none of the obstructive cases of jaundice showed impairment of hepatic function. This suggests that the test should be of some value in the differential diagnosis of jaundice. In ten of the twelve cases

of exophthalmic goiter, definite impairment of hepatic function was observed. This was extreme in some cases. These were clinically severe cases, with basal metabolic rates ranging from +20 to +80 per cent (average +55 per cent). This observation is in agreement with the results of Boyce and McFettridge (1938), who used the hippuric acid test. There seems little doubt that this hepatic damage is a part of the pathologic changes of hyperthyroidism, although it has not yet received general recognition. The clinical value of the test depends on its power of testing one function of the liver which is independent of the excretion of bile. This information may be useful for the following purposes: 1. The demonstration of hepatic damage in diseases in which its presence is uncertain or unconfirmed; hyperthyroidism, pneumonia, after surgical operations and rheumatoid arthritis. 2. The detection or confirmation of hepatic cirrhosis. The test is of particular value when jaundice is slight or absent. 3. This is of value for the differential diagnosis of toxic from obstructive jaundice. The pigmentary tests are, in general, unreliable for this purpose. The cases of jaundice studied are too few to reveal the limitations of the test in this respect, but they did fail to show any disagreement with the results expected, as all the toxic and none of the obstructive cases showed impaired function.

Etiology and Prognosis of Achrestic Anemia.—Israëls and Wilkinson present six cases of achrestic anemia in which particular attention was paid to the pathologic changes in the bone marrow. All the patients are still alive. The marrow was studied by sternal biopsy. In all of them there was a true megaloblastic hyperplasia, a hyperchromic megalocytic anemia, free hydrochloric acid in the gastric juice and a variable response to liver therapy. Patients 4, 5 and 6 were young women. The latter group resembles in some respects the so-called pernicious anemia of pregnancy. None of the patients were pregnant, but their response to liver treatment was better than in the cases reported previously, and their progress raises the hope that the prognosis, like that of pernicious anemia of pregnancy, will also be better than that of the previous cases. The present patients are, on the average, younger (58, 42, 27, 20, 17 and 25 respectively) than the former ones but this does not clash with the suggestion that achrestic anemia is allied to pernicious anemia, as the latter disease is now known to occur at an earlier age than was formerly thought. Some workers find difficulties in the differential diagnosis of achrestic anemia. Vaughan (1936) classifies it with megalocytic anemia due to liver disease, but the authors state that the necropsies of their previously reported cases failed to show any lesion in the liver apart from the fatty changes common to all prolonged anemias. The changes in the bone marrow of achrestic anemia often show a mixture of normoblastic and megaloblastic hyperplasia—corresponding to the partial response to liver—which is not like that of pernicious anemia in relapse. If the Price-Jones curve is thought to reflect changes in the marrow, it is not surprising that the curves of achrestic anemia do not at all times resemble those of pernicious anemia in relapse. Dyke and Young (1938) think that achrestic anemia is related to megalocytic hemolytic anemia. In hemolytic anemias the marrow shows an exclusively normoblastic hyperplasia. However, the chief difficulty has been the differentiation of achrestic and aplastic anemias. This confusion apparently has two sources: the association of the classic symptoms of aplastic anemia with a hyperplastic marrow and the nomenclature of the erythroblastic cells. The sternal marrow biopsies now reported confirm the postmortem observations described earlier that the marrow changes in achrestic anemia resemble those of pernicious anemia. Achrestic anemia is due to some interference with the proper action of the anti-pernicious anemia liver principle on the erythropoietic tissues. The correct differentiation of achrestic anemia is important when treatment is considered. First specific anti-pernicious anemia treatment should be given; larger total doses are required than for pernicious anemia, but they should be spread over a long period. As the more highly purified liver extracts may not contain all the active material, it is better to give one of the less highly purified intramuscular extracts. Blood transfusion seems to be necessary for the majority of patients. For young women it may be necessary only to tide over a specially difficult period.

This may be contrasted with the treatment for aplastic or hemolytic anemias. Anti-pernicious anemia treatment is not indicated for either of these conditions; repeated transfusions are necessary in aplastic anemia, while in hemolytic anemia transfusion is often followed by a decision for splenectomy. Splenectomy has no place in the treatment of achrestic anemia.

Presse Médicale, Paris

48:465-488 (May 8-11) 1940

New Method of Therapeutic Impaludation. P. Mollaret and J. Schneider.—p. 465.

*Hematuria in Hemophilic Patients. P. Emile-Weil.—p. 468.

*Amebic Dysentery in the Army. M. Poirot.—p. 469.

*Treatment of Meningococcic Meningitis with Sulfanilamides. A. Rusesco, V. Voiculesco and A. Diaconu.—p. 471.

Hematuria in Hemophilic Patients.—Emile-Weil reports a case of hemophilic hemotogenic hematuria. A man aged 29 had had a large hemarthrosis of the left knee ten years before. He had the present hematuria for eight days with violent right lumbar pains irradiating toward the penis, accompanied by polyuria and vomiting. Following transfusion of 200 cc. of blood, the urine became clear in three days without gravel or sand. Blood calcium was normal and calciuria decreased. Roentgenography revealed an oval shadow, undoubtedly a calculus, at the level of the twelfth rib opposite the inferior calix of the left kidney. The patient recovered in two weeks. Hematurias in hemophilic patients are first observed as a rule between the ages of 10 and 30. Such hematurias are caused by latent renal lithiasis preceded by hemarthrosis which is accompanied by a considerable decalcification of the femorotibial epiphyses and other articulations that may be involved. For a stone to form there must be an anomaly of the renal canaliculi causing urinary stasis, in addition to the decalcification of osseous lesions and temporary hypercalciuria at the time of hemarthrosis. One should differentiate between hemophilic or hemophilo-hemotogenic hematurias and hemotogenic hematurias caused by physiopathologic processes other than lithiasis.

Treatment of Meningococcic Meningitis with Sulfanilamides.—Rusesco and his collaborators treated ten cases of epidemic cerebrospinal meningitis, eight with soluseptazine (a benzyl-sulfanilamide derivation) in a 6 per cent solution and two with serum and azosulfamide in a 2.5 per cent solution. Nine patients recovered and one died. Five were nurslings aged from 2½ to 11 months and the others ranged in age from 2½ to 13 years. The drug was administered intraspinally, intramuscularly and in one instance orally. The disease lasted from two to seven days. The benzyl-sulfanilamide derivative was administered in decreasing doses as the patients' condition improved. Single injections amounted to from 10 to 15 cc. intraspinally and from 10 to 20 cc. intramuscularly in nurslings and approximately the double of this amount in older children. The total dosage of the substance was from 15 to 23 Gm. in nurslings and from 25 to 34 Gm. in the other children. To avoid relapse, prolongation of treatment to fifteen days is advisable. The authors recommend treatment of meningococcic meningitis with sulfanilamides exclusively and suggest combining serotherapy only in case the sulfanilamide is not well tolerated. The study of the literature reveals that the statistics for intraspinal and oral treatment are equally favorable. Intraspinally treatment is advised on account of its rendering possible the immediate concentration of the drug in the cerebrospinal fluid even though of short duration and because in the opinion of some investigators the inflamed meninges have a diminished permeability to sulfanilamides. Oral treatment is advised on account of the rapid elimination of intraspinally injected sulfanilamide and on account of the possible occurrence of meningococcic septicemia and encephalitis. In the presence of renal impermeability, administration into the blood is preferable. Sulfanilamide treatment gives a higher percentage of cures than serotherapy, particularly in nurslings. One should bear in mind that there are different strains of meningococci, some sensitive to sulfanilamides and others to serum. Meningococcus B infection should be treated with sulfanilamide. In the course of sulfanilamide treatment cyanosis, cutaneous eruptions, digestive

upsets and changes in the blood picture may occur. It is wise to examine the blood picture from time to time and check the complications.

48:529-552 (May 22-25) 1940

Food Imbalance (Vitamin A Deficiency) in Relation to Calculus of Urinary Tract. G. Mouriquand, J. Rollet, V. Edcl, Pape and H. Tete.—p. 529.

Arsenotherapy in Massive Instilled Doses in Grave Puerperal Infection. A. P. Ramos and A. A. Montes.—p. 530.

*Procaine Hydrochloride Infiltration of Left Stellate Ganglion in Paroxysmal Tachycardia: Case. P. Vêran, R. Dubois and Chevrel.—p. 533.

*Sulfanilamide-Treated Human Plasma: Its Advantages in Emergency Transfusions. A. Bécart and B. Philippe.—p. 535.

Paroxysmal Tachycardia.—Vêran and his associates report the successful management of a case of paroxysmal tachycardia by procaine hydrochloride infiltration of the left stellate ganglion. The patient, aged 43, in whom the shock of bad news had suddenly induced an attack of tachycardia, rapidly grew worse with increasing dyspnea, anorexia, insomnia, an overpowering feeling of fatigue and extreme motor and mental excitement. Roentgenologic examination revealed enlargement of the heart. Various therapeutic measures, including intravenous injections of quinidine, failed. Procaine hydrochloride (10 cc. in a 1:200 concentration) was injected into the left stellate ganglion thirty-two days after the onset. Within twenty-three hours cardiac action had become normal and all symptoms of cardiac failure gradually disappeared. An electrocardiogram taken seven months later showed cardiac rhythm. The authors present electrocardiographic views taken before and after injection. They believe, however, that the use of procaine hydrochloride is determined not so much by laboratory evidence as by diagnosis based on long existing tachycardia, increased pulse and previous cardiac lesions. The interval of time (twenty-three hours) between the injection and the manifest signs of recovery is not regarded as unusual. They briefly review the six cases previously reported in the literature of the treatment of paroxysmal tachycardia by procaine hydrochloride injected into the stellate ganglion.

Sulfanilamide-Treated Human Plasma.—Bécart and Philippe, correlating their discussion with data obtained by previous investigators, appraised the value of human blood plasma treated with sulfanilamide in comparison with that of total blood and of artificial solutions, in emergency situations such as are created by the war. They described the laboratory technics involved, observed characteristics exhibited by the therapeutic solutions under discussion and stressed the bactericidal and bacteriostatic power of the medicated plasma. Sulfanilamide adds a satisfactory viscosity to the human plasma that is especially effective if injected rhythmically, either intravenously or intramuscularly. Possessing sterile properties, it cannot transmit infection. It requires no "grouping" like total blood and hence is free from agglutination accidents. It is not affected by conditions of temperature and can easily be transported where needed. Its usefulness seems to be enhanced by the observation that it does not deteriorate as rapidly as stored blood. The whole subject requires fuller investigation.

Giornale Ital. di Dermatologia e Sifilologia, Milan

81:197-414 (April) 1940. Partial Index

*Histopathology of Gonorrheal Vaginitis in Young Girls: Special Reference to Modifications of Vaginal Mucosa from Estrogen Treatment. P. Pinetti.—p. 325.

Ide's Test for Serodiagnosis of Syphilis. C. Marchi.—p. 343.

Histopathology of Gonorrheal Vaginitis in Young Girls.—Pinetti performed biopsies on the vaginal mucosa of five girls from 3 to 7 years of age suffering from acute gonorrheal vaginitis of one month's duration. Biopsy was performed before, during, at the completion and one month after discontinuation of the treatment, which consisted of hypodermic injections of estrogen up to a total dose which varied between 12,000 and 18,000 international units. Microscopic studies revealed the following alterations of the vaginal mucosa: acute inflammation, degeneration and regression of the epithelial cells, intercellular edema, partial or complete destruction of the epithelium, intraepidermic migration of a large number of polymorphonuclear leukocytes, moderate hyperplasia of the epithelium, edema of the subepithelial connective tissue, diffuse cellular polymorphous infiltration of the tissues, with predominance of plasma cells,

moderate hyperplasia of the lymphatic tissue, dilatation of the blood vessels and subepithelial hemorrhages. These alterations regress in the course of estrogen therapy and are replaced by hyperplasia, metaplasia and cornification of the epithelium; the infiltrated tissues regenerate, and plasma cells become rare and lymphocytes numerous. At the completion of the treatment, infiltration of the subepithelial connective tissue has completely disappeared; the vaginal mucosa exhibits epithelial hyperplasia and cornification, which regress in about one month, at which time the vaginal mucosa is normal for the age of the patient.

Lotta Contro la Tuberculosis, Rome

11:67-140 (February) 1940

*Modifications of Results of Serologic Tests for Tuberculosis During Tuberculin Reaction. M. de Marchi.—p. 67.

Early Results of Immunitary Specific Therapy of Exudative Pleurisy with Tuberculous Vaccine. M. Bassi and N. Carinci.—p. 86.

Complement Fixation Tests for Tuberculosis During Tuberculin Reaction.—De Marchi studied the behavior of the reaction of complement fixation, Meinicke and Takata-Ara flocculation reactions and Weltmann's reaction during the various phases of the intradermal tuberculin reaction in 102 cases of pulmonary tuberculosis of different clinical types in the course of a sanatorium regimen or surgical therapy. The tests were done before intradermal inoculation of 0.10 cc. of diagnostic anatumerculin and again twenty-four, forty-eight and seventy-two hours after. The author found that there was no relation between the intensity of the cutaneous reaction and the results, either positive or negative, of the serologic tests, which followed parallel curves during the course and at the end of the tuberculin reaction with early diminution and late increase of the figures in the curves. The Meinicke test is the most sensitive to the influence of tuberculin. Partial changes from positive to negative results of the serologic tests, or vice versa, and total inversion of the results of the four serologic tests in the same case during tuberculin reaction were rare. Such a total inversion of the four tests in the same case took place in only one out of 102 cases. The author concludes that tuberculin introduced in the body of a patient with tuberculosis lowers the immunity and produces changes in the organic reactivity of the type caused by reinfection or exacerbation of tuberculosis. The serologic tests correspond with the development of new foci of tuberculosis, as indicated by diminution of the number of antibodies, imbalance in the ratio of albumins and globulins, lowering of the threshold of heat coagulation of the blood serum and increased velocity of sedimentation of the erythrocytes. The variations in the organic reactivity are transient and disappear when the tuberculin reaction is over. The author points out the importance of carrying out serologic tests for diagnosis and prognosis of tuberculosis at a distance from the intradermal tuberculin test in order to obtain reliable results.

Deutsche Zeitschrift für Chirurgie, Berlin

253:325-434 (March 14) 1940

Criticism of Effect of Chordotomy from Anatomic Point of View: Study of the Spinothalamic Tract. M. Kuru.—p. 325.

Blood Gas Exchange and Quantity of Circulating Blood in Narcosis Induced by Intravenous Administration of N-Methyl-C.C. Cyclo-Hexamyl-Methyl Barbituric Acid and C.C.-Isopropyl-B-Bromallyl-N-Methyl Malonylureid. E. Derra and J. Korth.—p. 381.

*Roentgenoscopy in Acute Abdominal Disorders. O. Kapel.—p. 399.

*Treatment of Brown Giant Cell Tumors by Implanting Cortical Fragments Derived at Site of Operation. E. Hohlweg.—p. 427.

Roentgenoscopy in Acute Abdominal Disorders.—Kapel reports on the diagnostic value of roentgenoscopy, which he employed with and without contrast mediums in some 400 routine cases of acute abdominal conditions such as ileus, perforations in the gastrointestinal tract, involvement of the urinary tract, invagination, trauma and the presence of foreign bodies. In 120 cases of ileus, about half of which were conservatively managed, x-ray examination confirmed the clinical diagnosis. In several cases clinically unsuspected ileus was promptly discovered. In seven cases of pneumococcal and gonococcal peritonitis with obscure clinical pictures, extensive ileus was found. On the other hand, thirty-five cases of pathologic conditions clinically suspected as ileus because of the presence of the typical signs were roentgenologically found to be cases of pseudo-ileus. In some of these cases intravenous urography disclosed an

obstruction in the urinary tract. In fourteen cases of perforated ulcer, preoperative discovery of air in the peritoneal cavity was considered an indication to prompt surgical intervention. In eleven cases of intussusception, x-ray study with the aid of a contrast medium showed successful disinvagination taking place without recourse to narcosis. The author admits the possibility of roentgenologic error in the diagnosis of ileus involving the colon. He stresses roentgenologic study in the diagnosis of acute renal and ureteral calculus. Hematuria may often be absent from the clinical picture during onset. In 110 cases of obscure abdominal lesions no diagnostic aid was derived from roentgenoscopy.

Treatment of Brown Giant Cell Tumors.—Hohlweg reports five cases of osteitis fibrosa cystica successfully managed by curetting and then implanting small fragments of cortical bone substance derived from the site of the surgical intervention. Spongy bone substance was used only as a supplementary material in larger cavities. The procedure consisted in first fenestrating the bone and thoroughly scraping away all tumor growth. Extensive portions of the bone cysts were then removed, leaving only a shallow trough. Pieces of cortex obtained in the operative act were reduced to the size of a pea and closely packed into the bone hollow. The periosteum was then sutured together over the closely packed bone fragments as far as it could be done and the limb left in a plaster cast for from four to eight weeks. This procedure made unnecessary the invasion of any other part of the skeletal system and seemed to favor more rapid healing. The author briefly reviews the other surgical procedures employed in the treatment of brown giant cell tumors.

Klinische Monatsbl. f. Augenheilkunde, Stuttgart

104:369-472 (April 30) 1940. Partial Index

- Hemeralopia in Soldiers. K. vom Hofe and M. Glees.—p. 369.
Color Vision in Street Traffic. K. Velhagen.—p. 377.
Relapse of Tuberculous Eye Disease. W. Hallermann.—p. 387.
New Endeavors in Fight Against Tuberculosis of the Eye. W. Wegner.—p. 395.
*Value of Tuberculin Test According to Mantoux in Diagnosing Tuberculous Etiology of an Eye Disease. H. Schlichting.—p. 401.
Subretinal Liquid in Melanosarcoma of Choroid. P. Cibis.—p. 424.

Mantoux Test in Diagnosing Eye Disease.—By intracutaneous injections of human and bovine tuberculin in eighty-seven cases of nontuberculous and eighty-seven cases of possibly tuberculous disease of the eye, Schlichting determined the weakest tuberculin concentration capable of causing a positive reaction. The author observed that (1) there was no essential difference between the human and the bovine tuberculin as to action, (2) the reactions of the two groups did not differ essentially and (3) the majority of tuberculous patients reacted negatively or their reactions became positive only with higher tuberculin concentrations. The author concludes that the Mantoux test is not suited for the diagnosis of the tuberculous etiology of diseases of the eye.

Medizinische Welt, Berlin

14:497-520 (May 18) 1940. Partial Index

- Conjunctival Disorders: Differential Diagnosis and Treatment in General Practice. R. Braun.—p. 497.
*Question of Epidemiology and Pathogenesis of Acute Pneumonia on Basis of 1,002 Cases. G. Wiele and H. Ibeling.—p. 500.
Psychotic Disturbances in Patients with Decompensated Heart Disease. W. Lueg and R. Weber.—p. 505.
Chediak's Dry Blood Test for Syphilis and the Meinicke Clarification Reaction II. E. Zimmermann.—p. 507.
Role of Urea in Modern Treatment of Wounds. J. Husslein.—p. 508.

Epidemiology and Pathogenesis of Acute Pneumonia.—Increased incidence of acute pneumonia with high mortality induced Wiele and Ibeling to investigate its pathogenesis and epidemiology. Their studies were made on 1,002 patients with acute pneumonia who were admitted to the Krupp Hospitals. The disease was especially frequent among men of the ages between 35 and 45. Morbidity as well as mortality were lower among women and children. Graphic records of the morbidity and mortality rates throughout the different months of the years from 1935 to 1939 inclusive indicate a great increase during the winter months and a low incidence during the summer months. It is suggested that the greater number of sunlight hours and the higher vitamin content of the organism play a part in the

defense against the infection and thus are important factors in lowering the incidence during the summer months. Cold with its action on the vascular system causes changes in the blood perfusion of the lung and it is assumed that cold reduces the resistance so that pathogenic micro-organisms can exert their effect. The realization that exposure to cold plays an important part in the pathogenesis of pneumonia suggests certain prophylactic measures. Workers should be warned that it is dangerous to depart from the factory by bicycle or motorcycle immediately after the cleansing shower and if insufficiently clad. Similar carelessness in the course of sports should be warned against. Such exposures to cold often result only indirectly in pneumonia, the direct result being a catarrhal infection. Certain meteorologic changes are accompanied by increased incidence of pneumonia. The infectiousness of pneumonia is rejected by the authors on the basis of their clinical observations. Type determination of the pneumococci from patients of sixty-four different industrial establishments disclosed no evidence of transmission among the patients nor was evidence of infection demonstrable among the physicians or the nursing staff. The fact that a patient had a recurrence of pneumonia of the same type shortly after the first attack speaks against a prolonged immunity after pneumonia.

14:521-544 (May 25) 1940

- Accident and War Surgery. M. zur Verth.—p. 521.
Correlation of Incretory Glands. F. Utz.—p. 523.
Desensitization (Rational Bee Venom Therapy) with Apieosan in Rheumatism of Allergic Origin. E. Kirebner.—p. 528.
*Therapy of Hyperemesis Gravidarum in Practice. F. Holldack and Hildegard Holldack.—p. 529.
Results of Examination of Cancer Patients in Nuremberg During the Years from 1933-1934 to 1937-1938. M. Meyer.—p. 531.

Therapy of Hyperemesis Gravidarum.—The Holldacks used a preparation containing vitamin B₁ and a liver extract in the therapy of severe as well as mild cases of hyperemesis gravidarum. The treatment was successful in all nineteen cases in which it was employed. The preparation is available in ampules and the administration is by intragluteal injection. In some of the cases four injections were sufficient, whereas in one case six were necessary to effect complete cessation of the attacks of vomiting. The authors feel that one injection each on three successive days is the best mode of treatment. No other therapeutic measures are necessary in addition to the vitamin B₁ and liver therapy. Many of the women commenced to gain weight shortly after the treatment. The vitamin B₁ and liver therapy was effective also against nausea without vomiting.

Wiener klinische Wochenschrift, Vienna

53:395-414 (May 17) 1940. Partial Index

- Rare Causes of Sudden Death: Hemorrhage into Abdominal Cavity. H. Winkler.—p. 395.
Spectral Analysis of Eschars. F. X. Mayer and H. Pesta.—p. 397.
Electrocardiographic Examinations on Caisson Workers. W. Breu.—p. 400.
*Serum Prophylaxis in Tetanus. H. von Karnitschnigg.—p. 403.
Question of Race and Colonies. L. Rauter.—p. 405.

Serum Prophylaxis in Tetanus.—Karnitschnigg investigated the problem of serum prophylaxis on the basis of 34,314 injuries. Tetanus antitoxin was administered to 16,269 and was omitted in the treatment of the remaining number. None of the patients who had been subjected to serum treatment developed the disease, while of the other group twenty-nine did. Among these there were twelve fatalities. The effectiveness of excision of the edges of the wound must be rejected. It was not possible in nine (injuries from electric current and extensive excoriations), while in one case tetanus developed in spite of the excision. Serum prophylaxis of tetanus has certain disadvantages, such as the skin eruption with its unpleasant sequelae. But in the choice between these complications and tetanus there should be no doubt. The greatly feared anaphylactic shock can be avoided almost entirely if the rules regarding desensitization are followed. Only one case of shock was observed in the reported material. Different serums were used in order to study the disadvantages of the injection of antitoxin. It was found that serum reactions are associated with its protein content and that its reduction may presumably lessen the incidence of the serum disease. The author concludes that serum prophylaxis of tetanus is an essential part of modern wound therapy and that he would not dispense with it under any circumstances.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

80:1119-1180 (April 30) 1940

- Investigations on Rickettsial Diseases in Sumatra: Pathologic Anatomy of Mite Fever in Human Subjects. W. Kouwenaar.—p. 1119.
Influence of Staying in Cool Temperatures on Oxygen Saturation of Venous Blood and on Minute Volume in Persons Living in Tropics. W. Radsma and Go Giok Khoen.—p. 1140.
*Arakawa's Reaction. D. P. R. Keizer.—p. 1152.
Papillomatous Hypertrophy of Tonsils. J. Kuitman.—p. 1156.
Cylindroma of Upper Eyelid Probably Originating in Tear Gland. J. M. Lebeau-Manders.—p. 1159.
Poisoning by Bite of Sea Snakes. A. Fossen.—p. 1164.

Arakawa's Reaction and Maternal Beriberi.—According to Keizer, Arakawa demonstrated in 1930 a relationship between the peroxidase content of breast milk and the vitamin B₁ content of the maternal organism. Arakawa's test demonstrates whether peroxidase is present in adequate amounts. If the test is positive the blue color appears at once or within one minute; if the peroxidase content is extremely low, the time required is much longer or there is no coloration at all. In order to determine whether beriberi influences the peroxidase content of the milk, Keizer made tests on sixty-two nursing mothers. In nineteen the reactions were positive, in forty-three they were negative. Clinical observations indicated that thirty-two of the sixty-two women were free from beriberi but that thirty were not. Of the thirty-two women who had no clinical signs of beriberi, eighteen had a positive and fourteen a negative Arakawa reaction. Of the thirty with beriberi, one had a positive and twenty-nine a negative reaction. Nine of the thirty women with a history of or with clinical signs of beriberi had nurslings with noticeable signs of beriberi. The author instituted treatment with large doses of vitamin B₁ in women with a negative Arakawa reaction. He reached the conclusion that a positive Arakawa reaction excludes maternal beriberi; a negative one, although not always actually indicating maternal beriberi, can be changed into a positive reaction by the administration of large doses of vitamin B₁.

Acta Medica Scandinavica, Stockholm

104:235-426 (May) 1940. Partial Index

- Studies on the Causation of Experimental Gastroprival Pellagra: Therapeutic Experiment (II) with Preventive Parenteral Administration of Vitamin B₁, Riboflavin and Vitamin A, Separately and in the Combination Vitamin B₁+Vitamin A. S. Petri, F. Nørgaard and E. Bandier.—p. 245.
Pathogenesis of Bundle Branch Block and Other Preponderance Curves: On False and True Infarction Curves in Precordial Leads. V. Mortensen.—p. 267.
A Method for Quantitative Determination of Prothrombin in Plasma. O. Thordarson.—p. 291.
Cyanosis in Treatment with Sulfonamide Compounds. N. Svartz and S. Kallner.—p. 309.
*On Irreversible Functional Disturbances in Chronic Pellagra. F. Mainzer and M. Krause.—p. 321.
Indications for Operation in Cases of Gastric Disease. D. C. Balfour.—p. 337.
Sarcoidosis (Boeck), Lymphogranulomatosis Benigna (Schaumann); Observations on the Bone Marrow Obtained by Sternal Puncture. S. P. Lucia and P. M. Aggeler.—p. 351.
The Treatment of Schaumann's Disease with Intravenous Injections of a Lipoid-Containing Substance Extracted from Tubercle Bacilli, Possessing the Properties of Tuberculin: A Report of Two Cases. K. Hedén.—p. 386.

Functional Disturbances in Chronic Pellagra.—Mainzer and Krause define chronic pellagra as that stage of the disease in which the skin has reached the phase of hyperkeratosis, evidenced by dry or moist eczema, with or without pathologic pigmentation. The acute disorder occasionally disappears without treatment. The chronic type of pellagra cannot always be cured, even if the patient tolerates a high caloric diet rich in pellagra preventive factor. At a certain stage the pathologic changes probably become irreversible. Moreover, such patients have a marked tendency toward relapse, sometimes depending on and sometimes without relation to the diet. Some investigators interpreted this as an indication that pellagra is not an avitaminotic condition. Although starting from an entirely different point of view, the authors have reached conclusions of importance to this problem. In previous reports they demonstrated that small amounts of insulin (5 units) regularly cause a marked and prolonged lowering of the blood sugar level, frequently accompanied by severe clinical symptoms. This phe-

nomenon was attributed to a functional disturbance of the adrenals. The present report extends and confirms the previous observations. The authors demonstrate that hypersensitiveness to insulin of patients suffering from chronic pellagra persists independently of clinical improvement or cure of the disorder, whereas in acute pellagra clinical cure is apparently accompanied by a complete normalization of the insulin-blood sugar curve. They believe that sooner or later pellagra produces irreversible changes. In this case the clinical cure is nothing but a remission; the relapse represents an exacerbation. The authors think that these observations are important with reference both to the pathology of pellagra and to vitamin research.

Acta Pædiatrica, Stockholm

27:279-401 (May 1) 1940

- *Adrenal Hypertrophy in Infants: New Clinical Entity of Neonatal Period. R. K. Dijkhuizen and E. Behr.—p. 279.
*Investigations on Congenital Stenosis of the Pylorus: Its Treatment and Prognosis; Report of 107 Cases Reexamined from One to Twenty-Two Years After Treatment. R. Rinvik.—p. 296.
Roentgenologic Follow-Up Examination in Congenital Pyloric Stenosis After Manifest Stage. K. Andresen.—p. 334.
Poliomyelitis and the Meteorologic Environment. W. F. Petersen and A. Mayne.—p. 353.
Investigations on Growth of Children in Elementary Schools of Finland. A. Ruotsalainen.—p. 374.
Antituberculous Immunity Produced by BCG Vaccine. J. Zeyland and E. Piasecka-Zeyland.—p. 393.

Adrenal Hypertrophy in Infants.—Dijkhuizen and Behr relate histories of four infants presenting symptoms suggestive of intestinal obstruction. In the first, laparotomy failed to disclose an obstruction, and in the other three necropsy excluded intestinal obstruction, but it revealed a striking feature; namely, extremely large adrenals. Although in the first case necropsy was refused, it seems probable that it was also one of adrenal hyperplasia. This child had a perineal hypospadias and evidence of pseudohermaphroditism suggestive of adrenal hyperplasia. A few similar cases of adrenal hypertrophy have been recorded in the literature, and these children were also found to have suffered from intestinal disorders. Most of the patients were boys or pseudohermaphrodites. It is suggested that an increased activity of the cortical hormone was present in these cases. Further clinical, pathologic and experimental data are required to define and explain this new clinical entity of the neonatal period.

Congenital Stenosis of Pylorus: Treatment and Prognosis.—Rinvik reports investigations on 137 cases of congenital pyloric stenosis treated in the department of pediatrics of the State University in Oslo, Norway. One hundred and eighteen of the patients were male and nineteen female infants. Seventy-two patients were treated conservatively. If the three children who were moribund on admission and a fourth who died from a complicating cystopyelonephritis are disregarded, the conservative treatment had a mortality rate of 2.9 per cent (two fatal cases out of sixty-eight). The author points out that before 1933 the therapy was largely surgical, but since the introduction of eumydrine (atropine methylnitrate) there has been a considerable advance in medical treatment. In a total of forty patients who have been treated with eumydrine, recurrence has been observed twice. The average duration of hospitalization for patients treated conservatively has been reduced from eighty-nine to thirty-six days. Signs of intoxication following the administration of eumydrine are rare. Sixty-five patients were treated surgically; the mortality was 7.6 per cent (five fatal cases). The late prognosis has been evaluated on the basis of a follow-up from one to twenty-two years after treatment. Ninety-five patients were reexamined. It was found that there exists a certain amount of familial predisposition to pyloric stenosis in small infants (in ten of 107). The infants do not seem to have a neuropathic disposition as they grow up, but relatively often they suffer from enuresis. They have a certain predisposition to what is termed "constitutional diseases." The defective growth of infants with pyloric stenosis is soon regained, probably within the first year of life. The relationship between weight and height follows the average for normal infants. The x-ray examination showed changes in more than half of the cases, but these were not accompanied by changes in the gastric chemism and they may exist without subjective symptoms.

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MEDICAL CAREERS IN PUBLIC HEALTH

CHAIRMAN'S ADDRESS

HAROLD S. DIEHL, M.D.

MINNEAPOLIS

Physicians have always played leading roles in the initiation and development of public health work. Together with collaborating scientists they have contributed most of the scientific discoveries which have made the prevention of disease possible, and in cooperation with other public spirited citizens they have fostered movements to have these scientific developments incorporated into public practice. As a result, it has frequently been said that the medical profession, unlike any other professional group, has initiated and supported activities the object of which is to make its own services unnecessary.

By virtue of their training, physicians have occupied most of the positions of major responsibility in the field of public health work. Some of these have long been career positions on a full-time basis, but the majority of physicians engaged in public health work have been on a part-time basis and have had to depend primarily on the private practice of medicine for their livelihood.

In speaking primarily of physicians in organized public health work, I fully appreciate the fact that the individual physician engaged in the private practice of medicine is the one on whom most of the ultimate responsibility for carrying out the practices of preventive medicine and public health has always depended. As the diseases which can be controlled by administrative and sanitary measures are reduced and the so-called degenerative diseases, such as Bright's disease, cancer, mental illness and high blood pressure, which can be dealt with only on an individual basis, increase in relative importance, still more responsibility for prevention must be placed on the physician in private practice. Appropriate discussion of this role of the practicing physician in public health work will be presented by Dr. Grant Fleming in his paper on "Preventive Medicine in General Practice" later in this program.

Careers in public health have always attracted certain physicians who were interested in the prevention rather than the treatment of disease and who were challenged by the opportunities and the administrative problems involved in the control of disease among the population *en masse*. Opportunities for such careers, until relatively recently, however, have been limited in number and have been handicapped by political considerations, insecurity and inadequate compensation.

Expansion in public health work has proceeded at a steady pace in this country for two or three decades, but new impetus has been given to this trend over the past five years by the provision of new and larger funds for health work as a part of the federal Social Security program. Public health programs supported by these funds must have the approval of the United States Public Health Service or the Children's Bureau, and to a high degree approval of a project is conditional on employment of personnel who meet the standards of training and experience recommended by the Conference of State and Provincial Health Authorities and approved by the Surgeon General of the United States Public Health Service. This has resulted in a great increase in the number of public health positions throughout the country and has limited these positions to qualified persons desirous of careers in this field, instead of permitting them to be prostituted for the payment of political debts or used to help build political machines.

QUALIFICATIONS AND TRAINING

The first requisites for success in public health work, as in every other field, are superior ability, industry, sound judgment and vision. Ability includes, first, intelligence and, second, aptitude for the particular field of public health in which one wishes to specialize. For example, for administrative positions in the general field of public health one needs so-called administrative ability in order that his department will function smoothly and efficiently, but he also needs what is commonly called political ability in order to get support for and public cooperation with his program. In technical positions, scientific ability is of first importance.

Industry and earnestness of purpose are essential for success, but these may miss the mark if they are not tempered by sound judgment, or they may accomplish nothing more than a routine, treadmill sort of job unless they are inspired by visions of greater accomplishments and new horizons.

Most of the leading figures in public health work up to the present time received their education in the "school of experience." There were no other schools available to them. These public health pioneers with superior ability and singleness of purpose learned and learned well by doing. In the last analysis, education is something which the individual must acquire for himself. There will never be any substitute for experience in either medical or public health training.

Yet the individual starting his career in public health today has the decided advantage of being able to learn in advance certain technics, which will be "the tools of his trade," to analyze and learn from the accumulated experiences of others, and to study the methods and procedures which have proved effective and those which have been found wanting in public health work. All this should enable him to start with a better under-

From the Division of Medical Sciences, University of Minnesota.
Read before the Section on Preventive and Industrial Medicine and Public Health at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

standing of his job and to develop it more rapidly than would otherwise have been possible.

Public health training may be obtained in any one of several schools or university graduate departments of public health. The separate schools of public health usually have the more highly specialized educational and research programs; but they may lack the valuable contacts with other graduate fields of medicine and with other related divisions of the university, such as public health nursing, sanitary engineering, political science, sociology, journalism and public speaking, which are available in the training programs of the university graduate departments of public health.

Fellowships or so-called training stipends to enable qualified physicians to obtain public health training are available from Social Security funds through state departments of health.

Supplementary to the year in public health at the university, the prospective health officer needs a period of practical experience in health work under supervision. This is analogous to the internship, which has long been recognized as necessary for the completion of a sound medical training.

Advanced training in public health covering one or more additional years is available to those who have demonstrated special aptitude in the work and wish further training in order to specialize in some field of public health. Fellowships for such advanced public health training may be provided either by the Rockefeller Foundation or by the United States Public Health Service through state health departments, utilizing Social Security funds.

TYPES OF OPPORTUNITIES

Administrative Positions.—The major positions in practically all public health organizations are administrative in character, yet the duties and responsibilities are such as to make medical training as well as public health training and experience essential as basic qualifications. The Committee on Professional Education of the American Public Health Association recommends that the educational qualification of health officers include the completion of a course leading to the degree of doctor of medicine in a recognized medical school, at least one year's internship in an approved hospital including a service in communicable diseases, a preliminary period of supervised field experience in a well organized department of health, and at least one full academic year devoted to the study of public health in a suitable university.

Health officers assume responsibility not only for environmental sanitation, laboratory work, vital statistics and general administrative problems but also for the control of communicable diseases, including tuberculosis and venereal infections, in which treatment is frequently involved, and for the reduction of morbidity and mortality among mothers and infants, involving not only antepartum and postpartum advice but also in some programs actual delivery service for certain groups of the population. The health officer is responsible also for the development of health programs in special fields such as cancer control, mental illnesses, industrial hygiene, and the identification and treatment of crippled children. In certain localities the expanding programs for the provision of medical care for indigent and near indigent groups of the population are under the direction of personnel especially trained in public health and employed either by welfare or by public health agencies. Much of the professional service involved in these vari-

ous activities will always be provided by practicing physicians, but in addition a medical training is considered by health authorities to be not only desirable but essential as a background for the planning and execution of a modern public health program.

Most of the administrative positions in public health are with state, city, county or other governmental health agencies, although there are also a number of exceedingly important administrative posts in the United States Public Health Service as well as in various voluntary health agencies. Administrative positions may be in the general field of public health or in such special fields as maternal and child hygiene, communicable diseases, hospital or institutional administration, and mental hygiene.

Scientific Positions.—Various functions in the field of public health are technical in nature and require for their efficient discharge special scientific training and ability in a limited field. The more common of these fields are as follows:

Epidemiology: The study of the origin, the method of spread, and the control of disease constitutes the science of epidemiology. Success in epidemiology depends on skill in clinical diagnosis, keen observation and "common sense," as well as on the utilization of laboratory procedures, a knowledge of the epidemiologic characteristics of the disease concerned, and the statistical analysis of epidemiologic data. Every major health department has a staff of epidemiologists serving in this manner. Epidemiology is one of the major subjects included in the public health training course.

Laboratory Work: Public health departments have long been making laboratory diagnostic aids available to practicing physicians as well as to health officials for the control of such communicable diseases as diphtheria, tuberculosis, typhoid, meningitis, gonorrhea and syphilis. In recent years the typing of pneumococci has been added to this laboratory service, and recently several virus laboratories for the study of influenza have been established by the Rockefeller Foundation in connection with state departments of health. A few health department laboratories manufacture vaccines and serums for free distribution for the prevention and treatment of disease. It is being suggested also that health departments aid in the program for the control of cancer by providing pathologic examination of tissues submitted by practicing physicians. At least one state laboratory is now providing such service.

Vital Statistics: The collection and tabulation of birth and death records is a function of the health department. It is on the analysis of such data that the relative importance of public health problems can be judged and the effectiveness of control measures evaluated. Of especial significance are the various studies of morbidity which are being made by certain statistical workers in public health. Such studies provide important information concerning the health problems of the community and may suggest certain approaches to their control.

Research: Most progressive workers in the field of public health are carrying on studies to evaluate their own practices and procedures and to extend the range of fundamental information necessary for disease control. Personnel in laboratory, statistical and epidemiologic positions have greater opportunities to conduct such studies than those who are in administrative positions. In the National Institute of Health of the United States Public Health Service, large groups of scientists are devoting themselves exclusively to research studies

in the field of public health. All together such positions offer enviable opportunities to those who have the interest and ability for scientific investigation.

Clinical Positions: There is no sharp line of demarcation between what is ordinarily considered the province of public health work and that of clinical medical practice. In fact there are various fields of accepted public health responsibility in which the professional service is primarily, if not exclusively, clinical medicine. Most of these positions are in hospitals, such as the Marine Hospitals of the United States Public Health Service, or in tuberculosis or mental hospitals which are affiliated with state or local health departments. Most colleges and universities now have student health services which provide not only health instruction but also more or less complete medical service for their student populations. A few public health positions in this country, as in Canada, include responsibility for the medical care of the populace or at least the indigent portion of the citizens in the community. Certain health agencies also are providing consultants to cooperate with private physicians in the diagnosis and treatment of tuberculosis, cancer and obstetric and orthopedic conditions. Increasing services in the "twilight zone" between public health and clinical medicine are constantly placing greater clinical responsibilities on health officials.

PUBLIC HEALTH TEACHING

Teaching opportunities in schools of public health and in public health departments of medical schools are increasing rapidly. Most of these positions carry reasonably satisfactory salaries and permanent tenure and offer attractive opportunities for teaching and research. The qualifications for such positions include a good medical education, sound graduate training in public health and adequate and broad public health experience. In addition, one must possess ability as a teacher and have demonstrated scientific interest and achievement which will command the respect of his colleagues on the faculty. He should also have research interests which will contribute to his personal scientific development and will add to the store of scientific knowledge in his field.

Teaching positions are available also in many liberal arts colleges and teachers' colleges. Most of these are combined with responsibilities for the student health service.

HEALTH WORK IN INDUSTRY

The professional opportunities in the important and rapidly expanding field of health work in industry will be discussed in a special paper on this program entitled "Opportunities for Physicians in Industry," by Dr. Thomas L. Shipman.

COMPENSATION AND TENURE

Salaries for most administrative positions in public health range from about \$3,000 to \$6,000 a year. A few, on a full-time basis, fall below \$3,000, a moderate number range from \$6,000 to \$10,000, and a very few are in excess of \$10,000 a year. Scientific positions in public health work usually carry somewhat lower salaries than administrative positions, but they tend to be more secure from political interference. Clinical and teaching positions carry salaries similar to those of scientific positions. Positions in industrial medicine usually are on a somewhat higher salary scale than positions in official public health agencies.

Certain positions in public health, such as those in the United States Public Health Service, have always carried permanent tenure provided the individual's professional work continues to be satisfactory; but all too

many other positions, unfortunately, have been at the mercy of the political party in power. Gradually, however, through the efforts of both governmental groups and civic organizations, public health is being taken out of the field of politics until today relatively fewer positions in public health are insecure because of political influence. Some of the major positions in state and city health departments are still considered as political barter, but rarely are the staff positions in these same departments disturbed even when there is a change in the departmental chief.

SUMMARY

The recent and future expansion of public health work demands more urgently than ever before competent and well trained leadership from the medical profession.

This expansion likewise is providing increasingly attractive opportunities to physicians for careers in the public health field,

Graduate training in public health is available in several schools and university departments of public health.

A certain number of fellowships for public health training are provided by state health departments from Social Security funds and in special cases by the International Health Division of the Rockefeller Foundation.

RHEUMATIC PERICARDITIS WITH EFFUSION TREATED WITH SALICYLATES

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Salicylates have been used in the treatment of acute articular rheumatism for some sixty years, but there remain wide differences of opinion with regard to their usefulness and mode of action. Yet the use of the drug persists, and studies of its clinical applications are still being published. In the United States, clinical practice largely restricts the use of salicylates to the relief of acute rheumatic arthritis. In Europe, particularly in France, the salicylates are regarded as valuable measures in the treatment of the cardiac manifestations of rheumatic fever.

A number of careful studies made in this country beginning with one by Miller¹ in 1914 and continuing to that of Master and Romanoff² in 1932 show that the administration of salicylates does not reduce the frequency of cardiac complications of patients with rheumatic fever. Wyckoff, DeGraff and Parent³ demonstrated by electrocardiographic studies that the conduction disturbances which are evidences of rheumatic myocarditis are uninfluenced by salicylate therapy, although the drug may reduce the temperature to normal levels and maintain it there. Hanzlik,⁴ in an exhaustive review of the action and uses of salicylates, states that salicylate therapy has no effect on heart failure in rheumatic fever and that salicylates neither prevent nor cure cardiac complications. Their effect is nonspecific; the action is antipyretic and analgesic and can be achieved equally with aminopyrine and cinchophen. More

From the Medical Service (Dr. George Baehr), Mount Sinai Hospital.
1. Miller, J. L.: The Specific Action of Salicylates in Acute Articular Rheumatism, *J. A. M. A.* 63: 1107 (Sept. 26) 1914.
2. Master, A. M., and Romanoff, Alfred: Treatment of Rheumatic Fever Patients With and Without Salicylates, *J. A. M. A.* 98: 1978 (June 4) 1932.
3. Wyckoff, John; DeGraff, A. C., and Parent, Solomon: The Relationship of Auriculoventricular Conduction Time in Rheumatic Fever to Salicylate Therapy, *Am. Heart J.* 5: 568 (June) 1930.
4. Hanzlik, P. J.: Actions and Uses of the Salicylates and Cinchophen in Medicine, *Medicine* 5: 197 (Aug.) 1926.

recently Lian and Facquet⁵ concede that the therapeutic influence of sodium salicylate on the cardiac complications of rheumatic fever is slight.

Advocates of the specific action of the salicylates are represented by Daniélopou,⁶ who administers from 15

years. At that time one of us had under his care at the Mount Sinai Hospital a young boy gravely ill with rheumatic fever and pericarditis with effusion. He was orthopneic and cyanotic, his pulse rate was 132, and there was gallop rhythm. With the idea of reducing the fever and thus reducing that part of the cardiac acceleration caused by the fever, he was given large doses of salicylates. Within twenty-four hours not only had the temperature dropped to normal but the whole clinical picture had changed. The boy was comfortable, the dyspnea and cyanosis had largely subsided, and the pulse rate had dropped to 90. Uninterrupted improvement continued.

The response was so dramatic and encouraging that similar therapy has since been used in a dozen cases. In several cases in which cardiac tamponade was so severe that pericardial paracentesis seemed urgently indicated, salicylates were administered and the symptoms were promptly alleviated. Since employing this medication we have had no occasion to aspirate the pericardium of any patient with rheumatic pericarditis. The results have all been satisfactory. There has been rapid alleviation of a sense of oppression and anxiety and a return to a state of comparative well-being. Two of these cases are here briefly summarized, and their course and features illustrated graphically:

REPORT OF CASES

CASE 1.—J. P., a boy aged 13 years, with two known previous attacks of rheumatic carditis, for the two weeks preceding admission to the Mount Sinai Hospital had malaise, pain

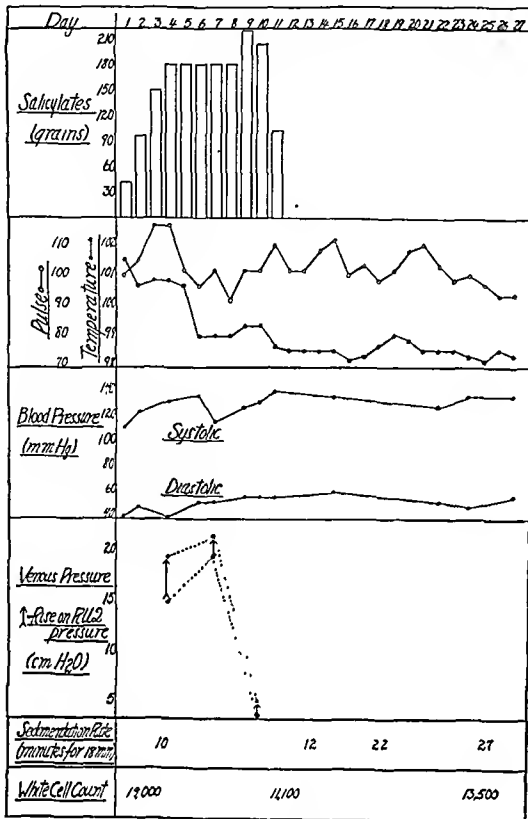


Fig. 1 (case 1).—Course of illness.

to 30 Gm. of sodium salicylate daily and who asserts that when the drug is given in adequate dosage within the first few days of the disease the heart may be spared. Most recently Bullrich and Sneider⁷ report the successful treatment of cardiac infection in rheumatic fever with from 16 to 23 Gm. of sodium salicylate daily given by rectum by the drip method. Their case reports do not give convincing evidence of beneficial action of salicylates on the cardiac lesion.

In spite of the controversy which now has extended over two generations, many competent clinicians still believe that the drug exerts a favorable action on the course of rheumatic fever. Coombs⁸ writes that "the administration of salicylate does limit the extent of the cardiac lesions"; Findlay⁹ states that he has no doubt that salicylates given in sufficient amount are veritable specifics against rheumatic arthritis, and White¹⁰ says that the drug "has a certain specific control of the rheumatic infection."

Our experience with salicylates in rheumatic carditis associated with pericardial effusion dates back some two

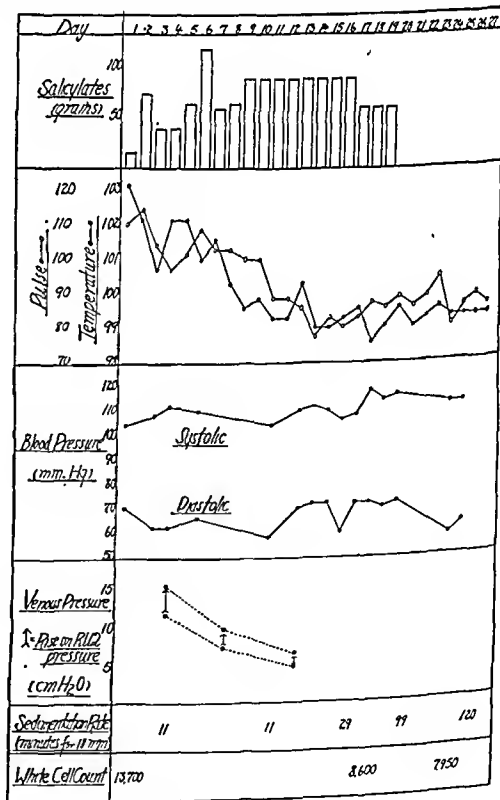


Fig. 2 (case 2).—Course of illness.

in the shoulders and chest, rise in temperature to 104 F. and profuse diaphoresis. Progressive dyspnea, orthopnea and cough developed. One day before admission he complained of precordial pain.

The boy was pallid and dyspneic with flaring alae nasi. Vessel pulsations were visible in the neck. Over the left lower posterior part of the chest there were dulness and bronchial

5. Lian, C., and Facquet, J.: Remarques cliniques et thérapeutiques sur le rhumatisme articulaire aigu, Bull. et mém. Soc. méd. d. hôp. de Paris 53: 1564 (Dec. 20) 1937.

6. Daniélopou, D.: Traitement du rhumatisme polyarticulaire aigu par les doses massives de salicylate, Presse méd. 31: 1045 (Dec. 15) 1923.

7. Bullrich, R. A., and Sneider, David: Reumatismo cardiaco primitivo, monosintomático, Bol. Acad. nac. de med. de Buenos Aires, August 1938, p. 285.

8. Coombs, C. F.: Rheumatic Heart Disease, New York, William Wood & Co., 1924, p. 323.

9. Findlay, Leonard: The Rheumatic Infection in Childhood, Baltimore, William Wood & Co., 1932, p. 162.

10. White, P. D.: Heart Disease, New York, Macmillan Company, 1931, p. 338.

breath sounds with bronchophony. The heart was markedly enlarged, in globular fashion. There was a systolic thrill at the base. Systolic and diastolic murmurs were audible at the apex, and a diastolic murmur was heard at the base. The heart sounds were distant. On percussion, hepatic dullness extended into the epigastrium.

The course and laboratory data are depicted in figure 1. He received large doses of salicylates, averaging from 150 to 200 grains (10 to 13 Gm.) a day, for eleven days. Objectively there was a sharp drop in the venous pressure, which is a direct reflection of the relief of the cardiac tamponade. Serial x-ray studies of the chest showed progressive diminution in the size of the cardiac shadow and resorption of the pericardial exudate. There was a sharp drop in the temperature curve. It is interesting that there was no demonstrable effect on the rheumatic activity per se as judged by the persistence of tachycardia, rapid sedimentation time of the red blood cells and leukocytosis. Subjectively the patient soon markedly improved, and on the fourth day he stated that he "felt better than ever before." On the tenth day, Kussmaul breathing developed and a blood carbon dioxide determination revealed that acidosis had developed. The drug was then stopped and these symptoms disappeared. The course of the disease after this followed the usual pattern of subacute rheumatic activity for weeks.

CASE 2.—B. C., a boy aged 14 years, had a noncontributory past history except for a tonsillectomy at the age of 8. The

resorption of the effusion, and a heart only slightly enlarged. Subjective improvement was even more striking. Within a few days he became very comfortable and much more alert. During the course of administration of the drug, evidence of salicylism in the form of ringing in the ears developed at one time, but this soon disappeared.

Ten other patients similarly treated all displayed a similar beneficial response to massive salicylate therapy.

COMMENT

Reports of the successful salicylate treatment of rheumatic pericarditis with effusion have appeared, chiefly in the French literature.¹¹ Paliard and Badenand¹² go so far as to state that in rheumatic fever unaccompanied by arthritic manifestations, but attended by pericardial involvement, the diagnosis rests on the rapid amelioration of the symptoms with salicylate therapy. Schultz¹³ found that occasionally the resorption of serous pericarditis and pleurisy was apparently hastened through the antixudative action of aminopyrine. Here again the activity of the underlying carditis was not allayed. Cassoute and his co-workers¹⁴ report rapid improvement and resorption of fluid in rheumatic pericarditis with effusion following the exhibition of the salicylates. Murray-Lyon,¹⁵ on the other hand, found no beneficial

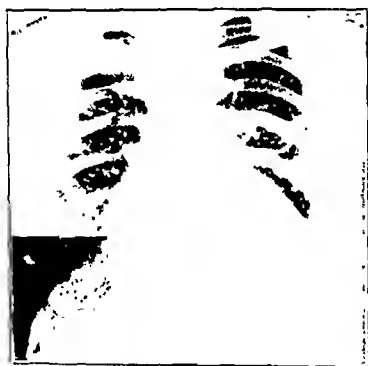


Fig. 3 (case 2).—Appearance on the morning after admission.



Fig. 4 (case 2).—Five days after admission.



Fig. 5 (case 2).—Twelve days after admission.

present admission to the Mount Sinai Hospital, his first entry, resulted from a train of symptoms dating back some four months. At that time he complained of unusual fatigue and dyspnea, followed by orthopnea and migratory polyarthralgias accompanied by a temperature of 100 or 101 F. Four days before admission there was a marked increase in chest and shoulder pain and the temperature rose to 102. This was attended by marked weakness and exhaustion.

The boy was tall, pallid, febrile and dyspneic. He complained of chest pain. The lungs were clear. On percussion the heart was markedly enlarged, being percussible 14 cm. from the sternum in the fifth intercostal space. The heart sounds were distant and of poor quality. A protodiastolic gallop rhythm was present. Apical systolic and diastolic murmurs were heard. The blood pressure was 104 systolic, 70 diastolic. The liver was palpable and tender.

The course and laboratory data are depicted in figure 2 and in the reproductions of roentgenograms. The progressive drop in temperature and venous pressure attendant on the administration of salicylates is evident. Objectively the changes in physical signs, corroborated by x-ray examination, were much more prominent. Four days after admission there was considerable diminution in cardiac dullness, so that whereas the heart had been percussible more than 2 fingerbreadths to the right of the sternum, it was now at the sternal margin. Figure 3 shows the x-ray appearance of the chest the morning following admission with the typical appearance of a pericardial effusion. Figure 4, taken five days later, shows marked decrease in the size of the cardiac shadow. Figure 5, taken one week later, shows even further diminution of the cardiac shadow,

effects of the drug in either the treatment or the prevention of rheumatic pericarditis.

The beneficial effects of salicylates on certain manifestations of rheumatic fever such as arthritis and pericardial effusion, and their apparent failure to stem the progress of other lesions such as endocarditis and myocarditis, may be related to the fact that arthritis and pericarditis represent exudative and the other lesions proliferative reactions to the rheumatic infection. Swift,¹⁶ after studying excised joint tissue in rheumatic fever before and after the administration of salicylates, concluded that "probably the most characteristic feature of this disease is the disappearance of exudation and the symptoms dependent upon it following the exhibition of sufficient doses of certain drugs" (i.e. the

11. Herman, P.: Contribution à l'étude des formes extra-articulaires de la maladie de Bouillaud, Thèse, Paris, 1929. Brodin, P., and Guyot, G.: Un cas de péricardite aiguë, primitive à gros épanchement vraisemblablement d'origine rhumatismale, Bull. et mém. Soc. méd. d. hôp. de Paris 47: 299 (March 2) 1931. Dimitracoff, C.: Péricardite exsudative et myocardite rhumatismale d'origine primitive, Arch. d. mal du cœur 27: 337 (June) 1934. Paliard and Badenand.¹²

12. Paliard, F., and Badenand, L.: La forme médiastino-pleurale de la maladie de Bouillaud, J. de méd. de Lyon 18: 205 (April 5) 1937.

13. Schultz, M. P.: The Use of Amidopyrine in Rheumatic Fever, Arch. Int. Med. 48: 1138 (Dec.) 1931.

14. Cassoute, E.; Giraud, Paul, Montus and Tissot: Péricardite primitive avec épanchement sans endocardite ni manifestations articulaires. Guérison par le traitement salicylé, Bull. Soc. de pédiat. de Paris 32: 425 (July) 1934.

15. Murray-Lyon, R. M.: Salicylates in Rheumatic Fever, Edinburgh M. J. 43: 84 (Feb.) 1936.

16. Swift, H. F.: Rheumatic Fever, Am. J. M. Sc. 170: 631 (Nov.) 1925.

salicylates). On the other hand, the proliferative response remains unaffected.

The relief of the cardiac tamponade following resorption of the pericardial effusion readily accounts for the prompt subjective and objective alleviation of the symptoms. The other cardiac lesions are a result of a proliferative process and consequently unresponsive to and unaffected by the drug.

SUMMARY

Salicylates given in large doses bring about prompt relief in acute rheumatic pericarditis with effusion. There result a rapid reduction in the pulse rate and a resorption of the pericardial exudate with quick relief of dyspnea and toxemia.

The salicylate action of pericarditis with effusion seems to be analogous to its action in arthritis with effusion. There are a rapid absorption of exudate and diminution in fever.

Salicylates exert no effect on the course of rheumatic infection or on the course of rheumatic endocarditis and myocarditis.

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SURGICAL TREATMENT OF HEMI-ATROPHY OF THE FACE

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Progressive facial hemiatrophy is a self-limited condition that always leaves in its wake a grossly apparent facial deformity. It is not a rare syndrome, and a bibliography of more than 400 articles reporting, often in detail, over 450 cases¹ shows that it has not been neglected by the medical profession. No specific treatment is known that will always stop the progress of the disease. It is remarkable, then, that few observations are available in the literature on the surgical repair of the inevitable disfigurement that results. It is our purpose in this paper to summarize the present knowledge of this condition and record our experience gained in six cases from surgical reconstruction with fat, fascia and dermal grafts.

DESCRIPTION

Hemiatrophy of the face may involve any or all of the superficial tissues, affecting skin, subcutaneous fat and muscles and at times bone and cartilage as well. The disease process starts in one or more focal points on the head and within a period of a few months to a few years may spread to involve the whole side of the face and scalp. Cases are reported in which the atrophy not only crossed over to the other side of the head but spread to the torso and limbs also. Characteristically, however, the disease is delimited to an area often suggestive of the distribution of branches of the trigeminal nerve. Involved skin frequently shows a brownish yellow pigmentation; owing to loss of subcutaneous fat and wasting of underlying muscles, the skin is depressed and sometimes adherent to the deep fascia. A sharp borderline often demarcates pathologic from normal tissue, an appearance at times so striking that it has given rise to the term "coup de sabre." Coincidentally

with atrophy of skin and subcutaneous fat there are generally, but not consistently, an associated fibrosis of arterioles and capillaries and a disintegration of sweat glands and atrophy of hair follicles, giving rise to patches of scleroderma and alopecia. The motor nerves are not affected. The cosmetic result of this condition, therefore, is that of a unilateral wasting away of a part or the whole of one side of the face, with some areas of the skin showing an unsightly brownish pigmentation and others a whitish sclerodermic atrophy. Patches of alopecia on the scalp and lack of development of nasal and aural cartilage or of the bony framework accentuate the disfigurement.

ETIOLOGY AND PATHOGENESIS

No one etiologic factor can be consistently demonstrated in all cases. In their monograph on facial hemiatrophy, Archambault and Fromm¹ report an incidence of antecedent injury in from 24 to 34 per cent of cases. Many times such injury, however, may have occurred years before the lesion was first noted. Since the disease most commonly starts in the first fifteen years of life a history of previous infection such as diphtheria, mastoiditis, local abscess or tuberculous cervical adenitis is frequently brought forth as the primary cause of the hemiatrophy. However, the high incidence of such infectious conditions in childhood makes it difficult properly to evaluate the etiologic role of such factors.

Cassirer² believed the pathogenesis of scleroderma and of facial hemiatrophy to be the same—a vasospasm of the sympathetic system. Archambault and Fromm, reviewing the more probable theories of pathogenesis, conclude "beyond a doubt" that involvement of the cervical sympathetic system alone frequently results in hemiatrophy of the face. They cite a series of ten cases in which hemiatrophy directly followed compression or injury of the cervical sympathetic system from such diverse causes as thyroid enlargement, cervical rib, tuberculous adenitis, cicatrix of the neck following burns, sarcoma of a cervical vertebra and trauma during a mastoid operation. They point out that the wide variation in the clinical syndrome can perhaps be explained on the assumption that separate trophic fibers run in the sympathetic trunks to the vasomotor and pilomotor systems and the organs of lacrimation and perspiration. The exciting pathologic state can be either irritating or paralyzing, and the result, therefore, is widely different in individual cases.

Cases of hemiatrophy are reported frequently as delimited by the sensory distribution of branches of the trigeminal nerve. It seems possible that such a distribution might be explained on a vascular basis, relating to areas affected by discrete vasospasm, since pain, paresthesia and anesthesia are relatively uncommon. Moreover, the removal of the semilunar ganglion does not produce the characteristic atrophic lesions.

It seems reasonable to conclude that hemiatrophy of the face most frequently results from infection or trauma causing injury to "some point, peripheral or central, of the sympathetic division of the 'vegetative' nervous system."¹

TREATMENT

The scarcity of observations on the treatment of hemiatrophy attests the present ignorance of the primary pathologic condition and the inadequacy of any present therapy. Treatment might properly be divided into three phases: (1) investigation of the underlying

From the Plastic Clinic of the Massachusetts General Hospital.
1. Archambault, La Salle, and Fromm, N. K.: *Progressive Facial Hemiatrophy*, Arch. Neurol. & Psychiat., 27: 529-584 (March) 1932.
Merritt, Katherine K.; Faber, H. K., and Bruch, Hilde: *Progressive Hemiatrophy of the Face: Report of Two Cases with Cerebral Calcification*, J. Pediat., 10: 374-395 (March) 1937.

2. Cassirer, Richard: *Die Vasomotorisch-trophischen Neurosen*, Berlin, S. Karger, 1912.

condition, (2) treatment of the local manifestations while the disease is in progress and (3) treatment of the final deformity resulting from this condition.

1. Investigation of the Primary Pathologic Condition.

—Pathologic change of the cervical sympathetic system should be suspected in every new case, and conditions that can be eliminated surgically must first be ruled out. Careful examinations must therefore be made for infections, tumors, congenital cysts of the neck and bony anomalies of the spinal vertebrae and face. When such factors cannot be discovered, an evaluation of the vasospastic component of the condition is indicated. Sometimes the cold and clammy appearance of the cutaneous area involved suggests the role of vascular spasm. A biopsy of affected skin may show a relative endarteritis similar to that seen in Raynaud's disease. Cutaneous temperature recordings may show a definite and satisfactory increase after foreign protein shock or procaine hydrochloride block. Such observations suggest that cervical sympathectomy may check the course of the disease. It has been pointed out,³ however, that if the condition has already progressed to the stage of fibrosis,

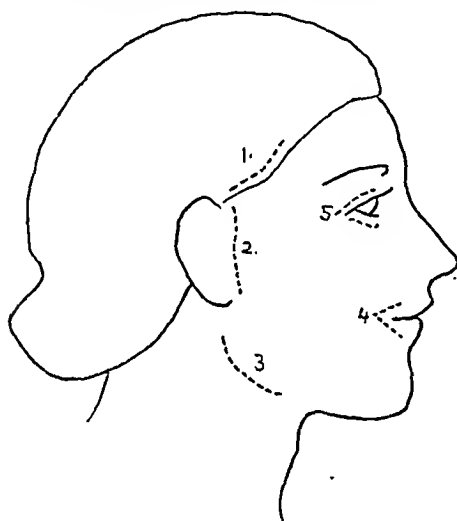


Fig. 1.—Incisions used for introduction of dermal grafts.

strangulation and destruction of capillaries and arterioles there will be no value in any such vasodilating procedure.

2. *Treatment of Local Manifestations.*—Localized patches of scleroderma are frequently but not consistently present as a component of the syndrome of hemiatrophy of the face. The literature is replete with a variety of treatments suggested for this condition. Perhaps the most logical approach is, again, that of sympathectomy in cases that exhibit features of vasospasm.⁴ Oliver and Lerman⁵ used injections of solution of posterior pituitary with benefit in some cases, believing that this effect resulted from active exercise of the peripheral vascular system through sympathetic stimulation. Reports of hypercalcemia associated with scleroderma have led some observers to advocate para-

thyroidectomy⁶ or ketogenic diets.⁷ Little attention, however, is now paid to the latter procedures.

3. *Treatment of the Final Deformity.*—Inorganic materials such as paraffin or white petrolatum in oil at one time were injected subcutaneously to fill in the defects. These materials not only cause permanent disfigurement but also set up inflammatory changes in the tissues and have been wholly discarded.

Autogenous transplants of bone, fat, fascia and skin are available for this purpose. Underlying maldevelopment or atrophy of the bony framework may make transplantation of bone a necessary step. As a rule, however, the major defect is the loss of subcutaneous fat.

Moszkowicz⁸ took long strips of fascia lata with the overlying fat attached in a case of hemiatrophy. With a large trocar, tunnels were made under the skin of the cheek through a small incision in front of the tragus and the fascial strips were then threaded into the tunnels through the trocar. By this method the thin transplant strips were prevented from sagging into a lump as they were each deposited into individual grooves made by the trocar, with septums of tissue intervening. He stressed the importance of overcorrection of the deformity to take into account the later resorption of the fat.

Eitner⁹ overcame the resorption that results from free transplantation of fat by developing from the temporal region an "island" flap of skin and fat. An isolated island of skin of full thickness, attached only to its pedicle of fat, was brought down from the forehead and introduced beneath the depressed skin of the cheek. The broad base of the pedicle insured a good blood supply, and the result was said to be excellent after three months. This ingenious procedure, however, is obviously limited to cases in which hemiatrophy is sufficiently localized so that normal skin and fat are available in an adjacent region.

Cotton¹⁰ reported one case of hemiatrophy in which finely cut gluteal fat in large quantity was found satisfactory. Such finely subdivided fat grafts made it possible to model smoothly the edges of the transplanted tissue in the area of the defect where the skin was undermined. In this case, surprisingly enough, there resulted no marked resorption or atrophy of this tissue during the four years the patient was followed.

An experimental study on animals of the behavior of free fat transplants (Gurney¹¹), however, leads to conclusions that do not corroborate Cotton's experience. In this work Gurney concluded that (1) multiple pieces of fat do not survive as well as one large one; (2) trauma to the graft definitely lessens its ability to survive; (3) a slight amount of oozing in the recipient area definitely lessens the viability of the graft; (4) fat is not replaced by scar tissue but the shrinkage is due to phagocytic action, and (5) only from one fourth to one half of the original fat transplant survives at the end of one year.

Free transplants of dermis and fat have been used in repairing small defects (Straatsma¹²). The possibility of the formation of small dermoid inclusion cysts

3. Mayo, W. J., and Adson, A. W.: Raynaud's Disease: Thrombo-Angiitis Obliterans and Scleroderma: Selection of Cases for and Results of Sympathetic Ganglionectomy and Trunk Resection, *Ann. Surg.* **96**: 771-783 (Oct.) 1932.

4. Brown, G. E., Craig, W. M., and Adson, A. W.: Selection of Cases of Thrombo-Angiitis Obliterans and Other Circulatory Diseases of the Extremities, for Sympathetic Ganglionectomy, *Am. Heart J.* **10**: 143-155 (Dec.) 1934.

5. Oliver, E. L., and Lerman, Jacob: Scleroderma Treated with Injections of Posterior Pituitary Extract, *Arch. Dermat. & Syph.* **34**: 469-477 (Sept.) 1936.

6. Leriche, René; Jung, Adolphe, and De Bakey, Michael: Surgical Treatment of Scleroderma, *Surgery* **1**: 6-24 (Jan.) 1937.

7. Kennedy, R. L. J.: Calcinosi and Scleroderma: Treatment of Case by Use of Ketogenic Diet, *J. Pediat.* **1**: 667-673 (Dec.) 1932.

8. Moszkowicz, Ludwig: Treatment of Hemiatrophy by Means of Fat Transplants, *Med. Klin.* **26**: 1478 (Oct. 3) 1930.

9. Eitner, Ernst: Cosmetic Surgery in Hemiatrophy of the Face, *Wien. med. Wchnschr.* **87**: 362-363 (March 27) 1937.

10. Cotton, F. J.: Contribution to Technic of Fat Grafts, *New England J. Med.* **211**: 1051-1053 (Dec. 6) 1934.

11. Gurney, C. E.: Experimental Study of Behavior of Free Fat Transplants, *Surgery* **3**: 679-692 (May) 1938.

12. Straatsma, C. R.: Use of Dermal Graft in Repair of Small Saddle Defects of the Nose, *Arch. Otolaryng.* **18**: 506-507 (Oct.) 1932.

was investigated by Peer and Paddock.¹³ These authors scraped the superficial epidermis with a razor, then excised small pieces with underlying fat and buried them subcutaneously. At intervals of one, two and three weeks and two, seven and twelve months biopsies were



Fig. 2 (case 1).—Preoperative appearance, showing right facial hemiatrophy, Oct. 18, 1923.

studied. This investigation showed that all hair follicles, sweat glands and sebaceous cysts degenerated and disappeared during the course of the experiment. In most sections, microscopic cysts lined with epithelium or encapsulated by nonepithelized granulating tissue were found. These tiny cysts were thought to result from incomplete removal of the epidermis and did not progress or enlarge during the course of a year.

OPERATIVE TECHNIC

On the basis of our experience with six cases of facial hemiatrophy, treated surgically for the correction of the deformity, the following points appear to be worth emphasizing:

1. *Selection of Recipient Area.*—A definite area is first decided on for reception of transplanted tissue. In our first case the temporal region alone was selected. In later cases increasingly larger areas were undermined, but care was taken to divide them into separate compartments so that if a complication developed about one graft the others would not necessarily be jeopardized.

2. *Incisions.*—The various incisions shown in figure 1 were chosen in order to give convenient access to the areas selected for grafting and to leave scars least likely to be conspicuous. We selected (1) for the temporal region, incision with the hairline; (2) for

the cheek, a vertical incision in front of the tragus, close to the anterior margin of the ear; (3) for asymmetrical jawline and chin, a curved incision behind the angle of the mandible; (4) for the corner of the mouth and lips, incisions at the mucocutaneous margins of the lips, and (5) for the orbital region, horizontal incisions parallel to the lid margins.

The most unfavorable of these incisions was found to be the fourth. Owing to the proximity and mobility of the mouth, it is difficult to keep the incisions dry, and the chance of sepsis is increased. Moreover, although scars along the vermilion border are inconspicuous, yet slight contractures near the corner of the mouth may alter considerably the pull of the oral muscles. In one case, that of a professional singer, the tightness of small scars near the angle of the mouth caused considerable discomfort.

3. *Undermining of the Skin.*—The tunneling under the skin is done by blunt dissection with scissors, and an effort is always made to find and follow the superficial facial plane where less bleeding is encountered. As emphasized by Gurney,¹¹ hemostasis is extremely important to the survival of transplants and it is important to have all active bleeding under control before the graft is introduced. The cavity is therefore packed tightly either with salt solution sponges or, if the bleeding is brisk from deep within the undermined area,



Fig. 3 (case 1).—Appearance after the first three transplantations of fat and fascia, April 6, 1926.

with gauze saturated with 1:1,000 solution of epinephrine hydrochloride. External pressure is then applied by the assistant while the transplant is removed from the donor site.

4. *Removal of the Transplant.*—For the purposes of transplantation we have used (1) fat alone, (2)

13. Peer, L. A., and Paddock, Royce: Histologic Studies on Fate of Deeply Implanted Dermal Grafts, Arch. Surg. 34:268-270 (Feb.) 1937.

fascia alone, (3) fat and fascia, (4) dermal graft and fat, and finally (5) dermal graft, fat and fascia in one block.

In our experience, transplantation of fat alone has been disappointing. The graft invariably diminishes

be used. With a skin graft knife a thin layer of epidermis is split from the donor site. The desired amount of tissue containing dermis, fat and fascia is then excised in a block. The defect is generally closed by swinging a pedicled flap of skin and fat from an adjacent area. If only dermis and a part of the fat layer are removed, the thin skin graft may be sutured back into place to cover the raw surface.

5. *Deposition of the Transplant.*—The transplant is then deposited in the recipient area either after cutting it in small cubes about 2 cm. in dimension or in one large piece. The former allows utilization of small skin incisions, but a single large block can be spread more evenly and secured in position more readily by means of "in and out" mattress sutures. These sutures are applied as follows: Mattressed silk stitches with long straight needles threaded on both ends are placed at the corners of the dermal graft. The needles are brought up through the skin of the face, and the sutures are tied over gauze at the desired points. Thus, if the region of the cheek has been undermined four sutures are placed, one at the zygomatic region, one on the side of the nose near the orbital ridge and the other two



Fig. 4 (case 1).—Appearance after six operations to correct facial atrophy, Feb. 10, 1928.

greatly in bulk and appears to be replaced by fibrosis. Contrary to other reports, we have not seen transplanted fat alone survive as adipose tissue.

It has been asserted that if the underlying fascia is removed with the fat from the donor area there is a better prospect for the viability of the fat. While our experience shows more encouraging results with this procedure, we feel that perhaps the additional degree of success, as contrasted with the results of fat alone, was probably due to the additional presence of the fascia.

Fascia alone seems to survive with the least amount of absorption. Where only a slight addition to the contour is necessary, as in the temporal or frontal regions or within the orbit, it has proved very satisfactory. In other areas it is often not possible to secure adequate amounts of fascia alone.

For more than two years we have utilized dermal grafts including fat and sometimes fascia in a block with promising results. Either the thigh or an elliptic area of the abdominal wall curving over the iliac crest is selected as the donor area. In obese patients, in whom the fat layer between dermis and fascia is often thicker than necessary, the lower part of the thigh may



Fig. 5 (case 1).—Appearance Dec. 8, 1939, twelve years after the last operation.

toward the lower border of the mandible. A Killian nasal speculum makes an ideal instrument to hold apart the two surfaces of the tunneled area and allows the needles to pass through the skin at the right places. In all our operations the dermal side of the transplant has been applied next to the skin.

6. *Closure and Dressing.*—The skin incisions are closed without drainage. External pressure is applied evenly over the entire side of the face with an elastic bandage. The patient is put on a liquid diet and not allowed to masticate food for ten days.

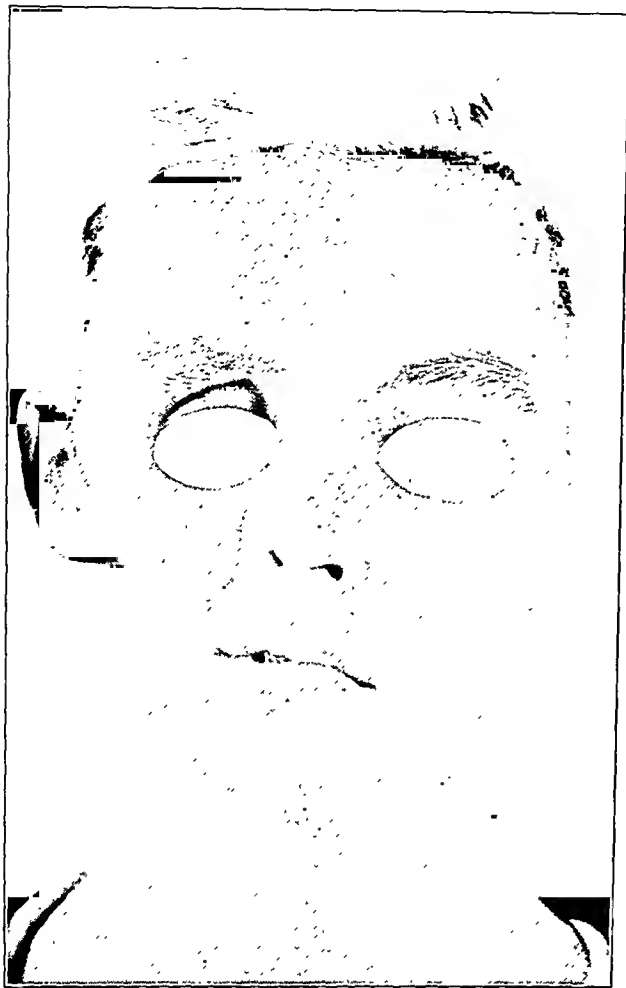


Fig. 6 (case 2).—Preoperative appearance, showing right hemiatrophy of the face, April 15, 1937.

7. *General Considerations.*—It is perhaps unnecessary to emphasize that extreme gentleness should be used in handling and shaping the transplant. Uncalled for crushing or trauma to the graft results in slough and necrosis. The nose and mouth cavities should be completely isolated from the surgical field. In one case an accidental puncture through the buccal mucosa led to infection and loss of the transplant.

We found that all types of graft which include adipose tissue undergo considerable absorption, and therefore overcorrection of the depression with one half to two thirds more tissue than apparently necessary is indicated.

Repeated operations must usually be performed in these cases. Although perfect symmetry of the face cannot be obtained, a satisfying degree of improvement may be acquired.

It is probably not without significance to note the change in outlook and mental attitude that often keeps pace with the patient's realization that a concrete and visible effort is being made to repair the defect. The possible significance of this is that, as a corollary to dropping an inferior attitude in their relation to society,

some of these patients begin to put on weight. The filling out of the face is not apparently limited to the normal side; gaining weight appears thus to have a salutary effect in maintaining the bulk of the transplant or checking its resorption.

This is well shown in both cases to be presented, the first and the last in the present series, summarized to bring out some of the points of treatment and operative technic previously discussed.

REPORT OF CASES

CASE 1.—E. M., a student nurse aged 26 years, was first seen in October 1923 with a complaint of right hemiatrophy of the face. No known etiologic factor is recorded in the history. Examination showed atrophy of the subcutaneous fat and muscles of the temporal region and cheek and over the mandible (fig. 2).

The first operation was performed Aug. 7, 1924. A transplant of fat only was removed from the anterior aspect of the right thigh and inserted beneath the skin of the right temporal region after this area was undermined through an incision at the hair-line. Wounds healed cleanly and she was discharged nine days later.

At the second operation, July 6, 1925, a block including fascia as well as fat was removed from the left thigh and transplanted



Fig. 7 (case 2).—Appearance after the first transplantation, Feb. 2 1938.

under the skin of the cheek through an incision in the right nasolabial fold. Sepsis developed in this transplant, necessitating drainage, and at discharge five weeks later the major part of the grafted tissue had been lost.

The third operation was performed six months later, Jan. 13 1926. An incision was made at the angle of the right mandible

and after the adhesions resulting from previous sepsis in the cheek had been freed a block of fat and fascia from the right thigh was inserted under the skin. The patient was discharged three weeks later with the wounds well healed.

At the fourth admission the previous transplants showed little resorption (fig. 3). At operation April 6 the previous



Fig. 8 (case 2).—Appearance after the third operation, March 24, 1939. Note that the patient shows a gain in weight manifested by a rounding out of the unaffected side.

scar in the cheek fold near the corner of the mouth was reopened, and fat from the right thigh was implanted in the cheek.

On Jan. 26, 1927, the patient was readmitted for the fifth operation. The old scar near the corner of the mouth was incised and a piece of fat and fascia measuring 3 by 1½ inches from the right midthigh was introduced, after blunt dissection, into the cheek.

At the sixth and last operation, Aug. 2, 1927, small pieces of fat and fascia were applied at the inferior orbital ridge and to round out the contour of the cheek.

When seen Feb. 10, 1928, the appearance of the face showed considerable improvement (fig. 4). On examination May 17, 1929, almost five years after the first operation, it was noted that the fat transplants in the cheek and about the eyelids had absorbed somewhat, but the result was considered reasonably satisfactory.

The patient was then not seen for ten years. When we saw her on Dec. 8, 1939, fifteen years after the first operation, it was found that over this period a good deal of the fat and fascia transplant had resorbed (fig. 5). However, in comparison with her original pictures there was considerable improvement.

CASE 2.—History.—E. W., an intelligent girl of 14 years, was first admitted to the Massachusetts General Hospital July 1, 1934, with the complaint that the right side of her face had

become progressively sunken through the last two years. When 6 years old, six years before the onset of any noticeable change, she struck her right forehead against an iron brace severely enough to lose consciousness. The past history included measles, chickenpox, whooping cough, scarlet fever and a tonsillectomy performed at 11 years. The family history was irrelevant. In December 1931, one week after recovering from bilateral pink eye, the patient first noted a white patch beneath the right eye. This patch became elevated like a callus, then peeled. Shortly after this a similar patch appeared on the right side of the forehead, and from then to the present there had been a gradual painless shrinking away of the tissues on the right side of the face.

Physical Examination.—On admission this well nourished girl appeared essentially normal except for the lesion on the face. She showed an area of alopecia and scleroderma above the right temple in the middle of which appeared an old scar. The skin of the right forehead was paper thin, nonadherent and brownish. Another patch of scleroderma lay beneath the right eye. Discoloration of the skin with atrophy of subcutaneous tissue, muscles, bone and cartilage extended to the midline and vertically down the nose to the chin. The tongue showed atrophy on the right. All cranial nerves were normal to rough tests. The pupils were equal, ocular movements normal and all reflexes normal. Although the distribution corresponded fairly closely to that of the fifth nerve, there was no sensory impairment.

Investigation of Primary Pathologic Change.—On admission the red cell count was 4,280,000, white cell count 4,800, hemoglobin level 85 per cent and smear negative. The basal metabolic



Fig. 9 (case 2).—Appearance Oct. 6, 1939, showing that a certain amount of resorption, especially of the transplants to the eyelids, has taken place. Otherwise the contour of the face is fairly satisfactory.

rate July 16 was —18 and when repeated —29. Spinal fluid examination gave a total protein of 32 mg., sugar 745 mg. and colloidal gold 0000000000, the Wassermann test was negative and there were no cells. The electrocardiogram was normal.

The skin temperature taken July 20 on contrasting points on opposite sides of the face was lower on the affected side, being

from 92 to 94 F. on the right and from 93 to 95.5 F. on the left. After procaine hydrochloride block of the right semilunar ganglion, the readings were from 95 to 95.5 F. on this side.

The skin temperature recorded three years later, however, appeared to show that the affected side was warmer than the other. Preganglionic sympathectomy, therefore, apparently was not indicated, nor was an arterial stripping operation.

Blood chemistry studies showed that sugar, urea nitrogen, nonprotein nitrogen, cholesterol and calcium levels were all essentially normal.

The patient was given one fourth grain (0.016 Gm.) of thyroid three times a day with no improvement.

X-ray study of the skull showed a rather broad and shallow sella turcica, no definite erosion of the clinoids, and no evidence of disease of sinuses. The chest plate showed an increased density of the bronchial tree, with questionable evidence of healed apical tuberculosis.

Biopsies of comparable areas from both sides of the face were examined. In the abnormal piece no subcutaneous fat nerves were seen, in contrast to the small nerve fibers running through the fat in the control specimen. Sweat and sebaceous glands and smooth muscle, however, were present in the abnormal piece, although not as plentiful as on the unaffected side. The blood vessels appeared to be similar in the two pieces.

Treatment of Local Manifestations.—On August 1 daily injections of 1 cc. of solution of posterior pituitary were started. After four months of almost constant treatment, the discoloration was less and the quality of the skin was definitely improved.

Treatment of Final Deformity.—On readmission July 15, 1937, there was found to have been no progression of the atrophy (fig. 6).

First Operation, July 23: A 2 inch incision was made anterior and inferior to the tragus on the right. The cheek was undermined toward the corner of the mouth. A second incision half an inch long was made above the hairline over the right temple, and a tunnel was undermined down to the superior edge of the zygoma. A thick split graft was then removed from the anterior surface of the left thigh, and a full thickness of lower dermal layer, fat and fascia was excised *en bloc*. The transplant was divided and threaded into the two tunnels previously prepared. Through and through stitches were used to maintain its position. The rectangular defect of the thigh, measuring about 2 by 3 inches, was closed by swinging a pedicled flap from adjacent tissue under some tension.

On readmission six months later, Feb. 21, 1938, very little resorption of the graft had taken place (fig. 7).

Second Operation, February 24: A large split graft was removed from the right thigh and a block of tissue including the lower layer of dermis, fat and fascia lata was excised. The dermal-fascial graft was cut into cubes measuring 1.5 cc. each. Through a small incision anterior to the right tragus the superficial tissues were undermined to the corner of the mouth and this tunnel was filled with transplants. A second incision lateral to the mandibular symphysis allowed other cubed transplants to be inserted above and below the angle of the mouth. The thigh wound was closed with plastic incisions. The grafts were not sutured in place. Immobilization of the face and jaw was obtained with elastic bandages.

On readmission six months later, September 14, the transplants appeared to be holding well.

Third Operation, September 15: After removal of a block of tissue from the left thigh, including fascia, fat and dermis, cubes of this tissue were packed into two areas, one beneath the angle of the jaw and the other beneath the lower lid extending to the bridge of the nose.

On readmission six months later, March 24, 1939, the grafts showed little resorption (fig. 8).

Fourth Operation, March 25: Through a 2 inch incision above the right parietal region, the atrophic discolored skin of the right side of the forehead was completely undermined to the eyebrow. A thin plaque of fascia carrying a small amount of fat was carefully spread in this undermined area and held securely with through and through stitches at the corners. Smaller grafts of fat and fascia were inserted through small incisions above and below the right palpebral fissure. The eyelids were sutured together and released ten days later.

Examination October 6 showed that the most recent graft of fat to the orbital region had undergone considerable resorption. The older grafts to the region of the cheek as well had lost some of their substance. The result at this time, however, more than two years from the first operation, showed a reasonably satisfactory improvement in general contour (fig. 9).

SUMMARY

Treatment of facial hemiatrophy may be divided into three phases: the investigation of the primary pathologic change, therapy directed toward improving the local lesions and finally surgical correction of the resultant disfigurement.

In surgical reconstruction with fat, fascia and dermal grafts, in six cases of hemiatrophy, we have found certain points of value. Two cases—the earliest followed for fifteen years—emphasize some of these points.

CONCLUSIONS

1. Facial hemiatrophy is a self-limited condition, the etiology of which is obscure.
2. Reconstruction of the final deformity through the use of autogenous tissues is of value.
3. Considerable absorption of all types of free transplants takes place over a period of time.
4. Dermal grafts and fascia are found to maintain the necessary bulk better than fat transplants.
5. The results of plastic reconstruction in hemiatrophy of the face utilizing dermal grafts and fascia are definitely worth while.
6. In one case there was gradual but marked resorption of fat and fascia grafts over a period of fifteen years. It is felt that there is less chance of similar results with dermal grafts.

475 Commonwealth Avenue.

DERMATITIS FOLLOWING THE WEARING OF NYLON STOCKINGS

PRELIMINARY REPORT OF FOUR CASES

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A new commercial product brings with it the possibility that it may be antigenic to some one. On May 15, 1940, the long heralded Nylon hosiery appeared on the market. Within a period of one month I encountered four patients with severe acute dermatitis in the stocking distribution following the wearing of Nylon hose of one particular brand. Patch tests so far made suggest that the finish or the dye of the stockings rather than the Nylon yarn may be the cause of the dermatitis. Further tests wait upon the cooperation of the manufacturers. This note is made so that others may be on the lookout for similar cases and to call attention to the need, for the manufacturers, to warn the public of the possibility of reactions to this product.

REPORT OF CASES

CASE 1.—Mrs. M. W., aged 30, a housewife, consulted me on May 27, 1940. One week after wearing Nylon stockings for the first time she developed a severe pruritic folliculopapular eruption involving the lower extremities from the toes to the upper third of the thighs, where it stopped abruptly. On May 28 the legs and thighs became edematous and the papules had become tense vesicles. Shortly thereafter the follicular lesions spread to the buttocks, abdomen, arms, face and neck. With four weeks of bed rest, wet dressings, soothing lotions and sedatives the process gradually subsided, although eight weeks after the onset involution had not yet been complete. Patch tests

gave strongly positive erythematous vesicular reactions to a piece of the stocking which had been worn. A test with an undyed piece of Nylon fabric yielded a negative reaction. Patch tests with the residue of an ether extract of the finished stocking were positive.

CASE 2.—Mrs. F. H., a school teacher aged 33, reported that she had worn Nylon stockings for about a week and then developed an itching eruption of the legs and thighs. On examination there was a diffuse papular follicular eruption confined to the legs and thighs. Practically every hair follicle was involved. The eruption was intensely pruritic and was slow to disappear. Three weeks after its onset on the legs a papulofollicular eruption appeared on the forearms and neck. Patch tests made with the stockings which the patient had worn produced an erythematous follicular papular reaction in twenty-four hours. Patch tests with undyed Nylon were negative after forty-eight hours. Patch tests with the residue of an ether extract of the finished stocking gave a positive reaction.

CASE 3.—Mrs. Y. M., aged 30, a housewife, wore Nylon stockings for two days and developed an itching eruption of the thighs and legs. The eruption was erythematopapular and confined to the hair follicles. Patch tests were positive to the stockings which had been worn but negative to undyed Nylon. A patch test with an ether extract of the finished stocking was strongly positive.

CASE 4.—Miss L. B., aged 30, a saleslady, seen through the courtesy of Dr. Louis Cheskin, wore Nylon stockings for three days after shaving the legs and developed a pruritic folliculovesicular eruption of both legs and thighs. Soothing applications had little effect on the eruption but it gradually subsided in two weeks. Patch tests gave strongly positive reactions to the stockings which had been worn and negative reactions to the undyed Nylon. A patch test made with the residue of an ether extract of the finished stockings was strongly positive.

COMMENT

In all four cases here reported the stockings which caused the dermatitis were confined to one particular brand. In a personal communication the E. I. DuPont de Nemours Company stated that Nylon yarn is manufactured by it and sold to various mills, where the material is made into hosiery and then dyed and finished. It is understood that the same dyes are used for Nylon as are used for cellulose acetate material. According to Schwartz and Tulipan,¹ hosiery is often finished by treating with a softening agent such as a sulfonated oil, a soap or an oil emulsion. From the follicular nature of the eruption in each of the four cases it might be deduced that the offending agent was dissolved on the skin in perspiration and was absorbed through the hair follicles. These cases suggest that the dye or the finish is probably a primary cutaneous irritant.

CONCLUSIONS

1. Four cases of dermatitis of the legs and thighs followed the wearing of Nylon stockings made by one manufacturer.
2. Patch tests in all four cases gave strongly positive reactions to the finished product and to the residue of an ether extract.
3. Patch tests made with undyed and unfinished Nylon were negative.
4. These cases suggest that the dye or finish used in preparing the hose in question may have been a primary cutaneous irritant, while the Nylon itself is probably innocuous.

31 Lincoln Park.

1. Schwartz, Louis, and Tulipan, Louis: *A Text Book of Occupational Diseases of the Skin*, Philadelphia, Lea & Febiger, 1939, p. 402.

EXCISION OF PHEOCHROMOCYTOMA

FOLLOWING NEAR FATAL ATTACK OF PARONYSMAL HYPERTENSION

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AND

ELEANOR HUMPHREYS, M.D.

CHICAGO

Benign neoplasms arising from the medulla of the adrenal gland or of similar structure but occurring outside the gland in the retroperitoneal space are being reported with increasing frequency. In 1934 Belt and Powell¹ reviewed thirty-six reported cases, and by 1939 one of us (E. H.) was able to collect 103 cases in the literature. Most of the reports deal with postmortem observations. In 1922 Labbé, Tinel and Doumer² first described the clinical syndrome caused by these growths. In 1926 Vaquez, Donzelot and Geraudel³ were the first to make a clinical diagnosis of such a neoplasm and advise operation. The patient refused this and the diagnosis was confirmed later at necropsy.⁴ Charles Mayo⁵ was the first to remove successfully such a neoplasm causing the typical syndrome, but at the moment the

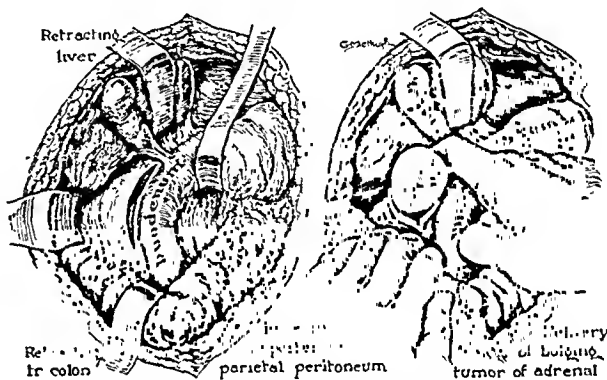


Fig. 1.—Semidiagrammatic illustration of excision of a pheochromocytoma in the right adrenal gland.

true nature of the tumor was not appreciated. The case reported by Pincoffs and Shipley⁶ in 1929 was the first instance of correct preoperative diagnosis, successful excision and prolonged survival of the patient.

The clinical syndrome caused by these growths is referred to as the adrenal-sympathetic or adrenal-medullary syndrome and may be briefly characterized as follows: In a previously healthy person there suddenly appear attacks of giddiness, weakness, blanching and pallor of the extremities, tachycardia, headache, precordial pain, often nausea and vomiting and partial or complete syncope. Blood pressure readings taken during the attacks show an increase of 100 mm. of mercury or more in the systolic pressure and marked increase in the diastolic pressure. There may or may not be hyperglycemia and glycosuria. The attacks last for from sev-

From the Departments of Surgery, Medicine and Pathology, the University of Chicago.

1. Belt, A. E., and Powell, T. O.: Clinical Manifestations of the Chromaffin Cell Tumors Arising from the Suprarenal Medulla, *Surg., Gynec. & Obst.* 58:9 (July) 1934.

2. Labbé, Mareel; Tinel, Jules, and Doumer: Crises solaires et hypertension paroxystique en rapport avec une tumeur surrénale, *Bull. et mém. Soc. méd. d. hôp. de Paris* 46:982 (June 23) 1922.

3. Vaquez, Henri, and Donzelot, Edouard: Les crises d'hypertension artérielle paroxystique, *Presse méd.* 34:1329 (Oct. 23) 1926.

4. Vaquez, Henri; Donzelot, Edouard, and Geraudel, Emile: Le surrénalome hypertensif, *Presse méd.* 37:169 (Feb. 6) 1929.

5. Mayo, C. H.: Paroxysmal Hypertension with Tumor of Retroperitoneal Nerve, *J. A. M. A.* 88:1047 (Sept. 24) 1927.

6. Pincoffs, M. C.: A Case of Paroxysmal Hypertension Associated with Suprarenal Tumor, *Tr. A. Am. Physicians* 44:295, 1929.

eral moments to several hours. Once developed they usually increase in frequency, may or may not appear to follow emotional or physical strain, or may be induced by bending the body in a certain direction. Fatal collapse may result from any one attack, especially if the attack appears to be induced by some trauma or emotional strain. It has been generally assumed that the

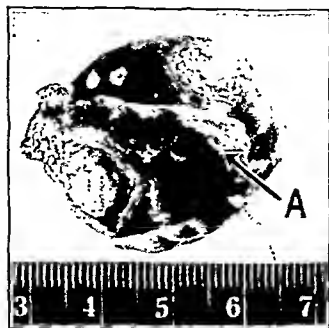


Fig. 2.—Appearance of the specimen. A spherical tumor bulged from each surface of the adrenal gland (A).

attacks are due to sudden liberation of epinephrine or epinephrine-like substances into the circulation by the tumor, which thus retains at least this much of the function of normal adrenal medulla. This point has finally been actually demonstrated by Beer, King and Prinzmetal.⁷ Since 1927 there have appeared in the literature reports of a number of successful surgical removals of these neoplasms, and in 1938 MacKenzie and McEachern⁸ collected fifteen instances from the literature, adding one case of their own. In 1938 we also reported such a case.⁹ Our purpose in recording the following case is to cite again the feasibility of successful removal of these neoplasms which, if not diagnosed and left untreated, result sooner or later in death from the attacks of severe circulatory disturbances which they engender. They are thus benign from the morphologic standpoint but physiologically malignant.

REPORT OF CASE

Mrs. F. H., a white woman aged 43, was admitted to the Medical Service of Dr. George F. Dick Sept. 24, 1935. At this time there were no serious complaints, and the following diagnoses were made: infected tonsils, simple goiter, small uterine fibroids and cervicitis. The blood pressure was noted as 130 systolic, 80 diastolic. She was readmitted to the hospital April 25, 1939, stating that she had had a thyroidectomy in September 1937 and felt quite well for the next six months but that in June 1938 she began to have attacks of severe headache and that in November 1938 an attack was characterized by severe headache, backache and "kind of unconsciousness." Another such attack occurred about Dec. 25, 1938, and again in February 1939. On April 20, 1939, the severity of the attack was extreme, being followed by a state of collapse which, when observed by the family physician in attendance, led to the pronouncement of death. As was his custom when his patients appeared to have just died, he administered an intracardiac injection of epinephrine. This was followed by a return of pulse and respiration; shortly thereafter, because of marked rales, the patient was "turned upside down" and a "quart of fluid" drained from the lungs. On admission the blood pressure was 140 systolic, 85 diastolic.

The patient was observed in the hospital until May 7, when at 3 p. m. she complained of nausea, vomited and had severe back pain, tachycardia, labored respiration and cyanosis. The intern called to see her observed the blood pressure to be 295 systolic, 155 diastolic, and pulse rate 160. In about one hour the attack passed off, the blood pressure falling to 160 systolic, 110 diastolic.

7. Beer, Edwin; King, F. H., and Prinzmetal, Myron: Pheochromocytoma with Demonstration of Pressor (Adrenalin) Substance in the Blood Preoperatively During Hypertensive Crises, *Ann. Surg.* 106:85 (July) 1937.

8. MacKenzie, D. W., and McEachern, Donald: Adrenal Pheochromocytoma: The Syndrome of Paroxysmal Hypertension, *Tr. Am. A. Genito-Urin. Surgeons* 31:127, 1938.

9. Brunschwig, Alexander; Humphreys, Eleanor, and Roome, Norman: The Relief of Paroxysmal Hypertension by Excision of Pheochromocytoma, *Surgery* 4:361 (Sept.) 1938.

A diagnosis of paroxysmal hypertension due to pheochromocytoma was made and operation advised. Because of the previous near fatal attack, retroperitoneal pneumograms were not deemed advisable.

On May 9, under procaine hydrochloride spinal anesthesia later supplemented by ethylene, the abdomen was entered through a high midline incision. The result of manual exploration was negative except for the right adrenal gland, which appeared to include a spherical, rather firm tumor mass about 4 cm. in diameter. The posterior parietal peritoneum was incised along the outer curvature of the upper portion of the second part of the duodenum, permitting retraction of the latter to the left. The tumor-bearing adrenal was then removed by blunt dissection (fig. 1). After hemostasis the posterior parietal peritoneum was closed and then the abdominal incision by interrupted silk sutures.

At the onset of the operation the blood pressure was 120 systolic, 60 diastolic. During manipulation of the tumor and its removal with the right adrenal the pressure rose to 270 systolic, 120 diastolic, and at the termination of the operation fell to 100 systolic, 60 diastolic. Venoclysis of physiologic solution of sodium chloride (1,500 cc.) was begun as soon as the tumor was removed. Convalescence was uneventful; the temperature was highest, 100 F., on the second and third days and normal thereafter. The pulse remained between 80 and 90 beats per minute. The patient has been seen on several occasions since discharge on May 24, 1939, and has remained well. The blood pressure is 100 systolic, 70 diastolic.

Pathologic Study: The gross appearance of the tumor is shown in figure 2. It weighed 13.5 Gm. Microscopic examination shows a typical pheochromocytoma, many cells of which reveal the positive "chromic reaction" (fig. 3).

A bio-assay by Dr. Louis Leiter on the anesthetized dog, comparing the rise in blood pressure following injection of a hydrochloric acid extract of a known quantity of tumor with

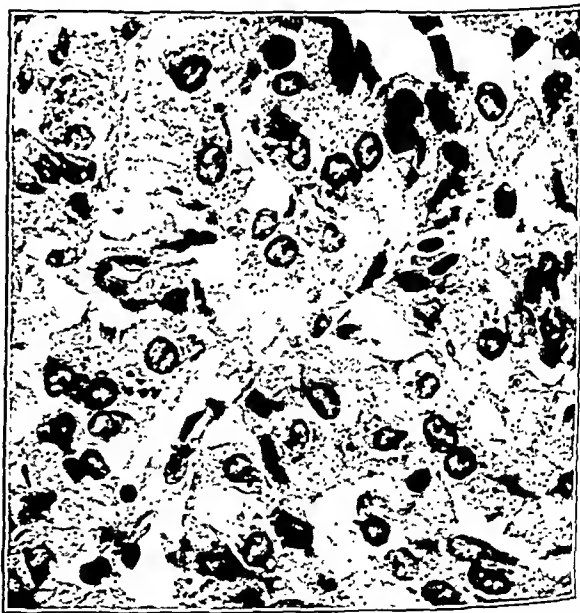


Fig. 3.—Section of the pheochromocytoma, showing typical large polygonal cells with hyperchromatic nuclei and finely granular cytoplasm; slightly reduced from a photomicrograph with a magnification of 1,300 diameters.

the rise produced by known quantities of epinephrine, revealed the epinephrine content of the tumor to have been approximately 2.2 mg. per gram.

COMMENT AND SUMMARY

Increased experience with the successful removal of pheochromocytomas of the adrenal producing paroxysmal hypertension emphasizes the importance of early

diagnosis to permit surgical excision prior to fatal collapse, which sooner or later ensues in patients with such neoplasms.

In the reported successful operations the manner of approach was about equally divided between abdominal and lumbar incisions. In our opinion the abdominal incision appears preferable because of the frequent inability to localize the tumors accurately prior to operation. Of the 103 reports (mostly of necropsies) reviewed in the literature forty-three concerned the right and thirty-four the left adrenal; there were thirteen instances of tumors in each adrenal, and in thirteen instances the neoplasms were entirely outside the adrenal glands.

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TYPES OF BURIED GRAFTS USED TO REPAIR DEEP DEPRESSIONS IN THE SKULL

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This paper embodies the clinical experience obtained from plastic operations on fifteen patients with depressions in the skull of varying degree. In seven of the cases there had been brain abscess or meningitis and the dura had been opened widely at the time of operation, exposing the brain. In three of the cases there was osteomyelitis of the frontal bone and the bone had been removed, exposing the dura, but the dura itself was not opened. In the remaining five cases there were depressed fractures of the frontal bone with the dura uninjured or only slightly lacerated.

Nine of the fourteen cases, from the standpoint of deformity, presented large depressions in the frontal region due to the removal of the bony brow, one or both frontal sinuses and an adjacent area of frontal bone. The remaining six cases exhibited less extensive depressions resulting from the removal of smaller areas of bone above the frontal sinuses or from the removal of a single bony brow. In none of the infected cases were depressions repaired until the wound had remained completely healed for a period of two years.

The two essentials for the repair of depressions in the skull are an adequate cutaneous covering and a satisfactory filling substance to replace the absent bone.

CUTANEOUS COVERING

The scalp skin was present in all of my cases although frequently separated by wide areas of scar tissue covered by a thin layer of epidermis. This was particularly true in the infected cases where the dura had been incised with subsequent herniation of the brain through the dural opening. A covering of skin was provided in these cases by first carefully dissecting the thin layer of epidermis from the underlying scar tissue covering the brain. Pulsations from the frontal lobe immediately beneath the layer of scar tissue sometimes made this procedure slow and difficult. The retracted scalp skin at the margin of the wound was then widely undermined and sutured to cover the defect completely. In a few cases it was necessary to form flaps of the scalp skin in order to obtain proper relaxation over the exposed area.

With a satisfactory covering provided there remained the much more difficult problem of selecting a suitable substance to insert beneath the skin overlying the depression. This suggests a discussion of the types of grafts used for burial beneath the skin.

FOREIGN SUBSTANCES

Many foreign substances have been buried beneath the skin to fill depressions in the skull and nose for the purpose of improving a person's appearance. These foreign substances include ivory, animal bone, silver and gold plates and paraffin. Unfortunately the human body resents the presence of foreign material, and when it is used there occurs a slow but progressive action in the surrounding host tissue which eventually results in expulsion of the implant. There are cases, it is true, in which foreign implants have remained in place for years, but local trauma or infection seems to remind the body of their presence and precipitate their removal. The harmful sequelae following the use of paraffin are well known, and its former wide application is now very generally condemned.

DERMAL GRAFTS

(Skin dermis with the epidermis removed). Loewe¹ and Rehn advocated the use of dermis as a buried graft in plastic operations prior to 1914. Rehn,² however, first applied it clinically in the treatment of post-operative hernia. Eitner³ in 1920 described a method of elevating a depression in the face by inserting a section of de-epithelized derma beneath the skin overlying the depression. Either omitted reference to the earlier work of Rehn and Loewe. Vilray Blair and J. B. Brown used dermal grafts and described the method to Straatsma,⁴ who successfully used the graft to repair saddle nose. Smith⁵ has used the dermal graft to repair saddle nose in a large number of cases and feels that in many respects it is superior to cartilage.

One would suppose, theoretically, that cyst formation might occur from hair follicles, sebaceous glands or sweat glands in the buried section of dermis. In order to determine the fate of these structures I buried sections of dermis and fat beneath the chest skin of human beings and removed them at intervals of seven days to one year.⁶ Examination of the sections of the implanted dermis showed that sebaceous glands and hair follicles completely disappeared. The sweat glands were present in the one year section but showed definite degenerative changes. Remnants of epidermis incompletely removed from the dermis at first formed small cyst cavities, but in the later sections these were entirely absent. From this evidence one may conclude that dermis is a good filling substance, since both the epithelial elements in the dermis and small remaining portions of epidermis tend to degenerate and disappear. Dermal grafts also become part of the living organism after transplantation and remain as living tissue.

To repair defects in the skull the dermal grafts can best be taken from the thigh, including the underlying fat and fascia lata. The epidermis is first shaved off

1. Loewe, O.: München. med. Wchnschr. 24: 1320, 1913.

2. Rehn, E.: München. med. Wchnschr. 1: 118, 1914. Rehn, E., and Miyauchi: Arch. f. klin. Chir. 105: 1, 1914.

3. Eitner, E.: Ueber Unterpolsterung der Gesichtshaut, Med. Klin. 16: 93 (Jan. 25) 1920.

4. Straatsma, C. R.: Use of the Dermal Graft in the Repair of Small Saddle Defects of the Nose, Arch. Otolaryng. 16: 506 (Oct.) 1932.

5. Smith, Ferris: Personal communication to the author.

6. Peer, L. A., and Paddock, Royce: Histologic Studies on the Fate of Deeply Implanted Dermal Grafts, Arch. Surg. 34: 268-290 (Feb.) 1937.

Read before the annual meeting of the Society of Plastic and Reconstructive Surgery, Philadelphia, during November 1938.

with a sharp Thiersch knife, and a pattern of dermis, fat and fascia lata is removed from this area. When a large graft is required two segments are removed and sutured together to form a complete pattern. Some absorption occurs in the fat layer over a period of time, but the graft adapts itself remarkably well to the



Fig. 1.—Cadaver rib cartilage graft preserved in alcohol for one month and buried beneath the chest skin of a female patient. The cartilage graft was removed after twenty months and sectioned. Note invasion of cartilage by numerous strands of connective tissue.

rounded contour of the skull. Where one desires to reconstruct a ridge such as a bony brow or bridge of the nose, cartilage is more desirable than dermal graft.

The dermal graft is indicated, therefore, to fill shallow depressions in the skull but is not suitable for the repair of a deep depression. In my series of fifteen cases the only two failures occurred where large dermal grafts were used which became infected after operation. The infected areas were drained early, but in both cases drainage continued until all of the dermal graft was extruded or removed with an instrument. The infections then promptly subsided. One of these failures was later successfully repaired by autogenous rib cartilage, but in the other case further operation was refused. Both infections were localized in the soft tissues of the scalp and did not lead to cerebral involvement.

RIB CARTILAGE PRESERVED IN ALCOHOL

Human cartilage preserved in alcohol was used rather extensively a generation ago to fill depressions in the nose. The procedure was discarded because of the belief that the grafts either suppurated or were absorbed and replaced by fibrous tissue. Recently there has been a revival of the method, and Pierce and O'Connor,⁷ J. B. Brown, Straith, Straatsma and I, among others, have

used preserved human cartilage grafts to fill depressions about the face and skull. Since all of the observations concerning the fate of these cartilage grafts were purely clinical, I buried sections of human pickled cartilage beneath the chest skin of other human beings and removed these grafts at intervals varying from seven days to two years.⁸ Histologic examination in the seven and eight day sections showed an early reaction in the host tissue surrounding the implants. There were numerous collections of giant cells, polymorphonuclear leukocytes and large and small round cells. A thick connective tissue capsule formed very early about the cartilage implant, walling it off from the adjacent host tissues. This reaction lasted about one month and then disappeared to a large extent. The cartilage grafts remained as tolerated dead foreign bodies until the end of the nine and one-half month period. From nine and one half months till two years after implantation the sections showed progressive invasion of the cartilage implant by fibrous tissue and partial absorption of the cartilage. From this experimental evidence one may conclude that pickled cartilage grafts undergo a slow, gradual invasion and absorption and hence are not as satisfactory a filling substance as fresh autogenous cartilage. However, when the patient will not consent to the removal of his own costal cartilage one may use fresh cadaver cartilage preserved in 50 per cent alcohol. The preserved cadaver cartilage is also useful in children where their own costal cartilage does not possess sufficient bulk to fill a deep skull defect or when the

patient's age or general condition precludes a long operation. My procedure is to remove the cartilage from alcohol and place it in physiologic solution of sodium chloride one hour before operation. The cartilage is then removed from the saline solution and inserted in a subcutaneous pocket beneath the abdominal skin, the wound is closed and firm pressure dressing is applied to prevent bleeding. If the patient tolerates the cartilage in the abdominal tissues it is removed at a later operation and inserted beneath the forehead skin to fill out the depression. I always hoard the cartilage first to be sure that the patient

will retain the foreign graft before placing it beneath the scalp. The pickled cartilage is surprisingly resistant to infection. I have had two infections at the abdominal

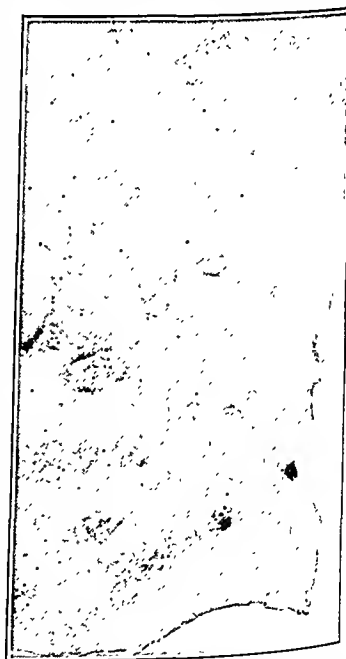


Fig. 2.—Autogenous rib cartilage graft buried beneath the chest skin of a human being for five years and ten months. Note complete absence of invasion by connective tissue and normal appearance of cartilage. (The specimen was sent to me for section and microscopic examination by Dr. Claire Straith.)

7. Pierce, G. W., and O'Connor, G. B.: *Ann. Otol., Rhin. & Laryng.* 47: 437-452 (June) 1938. (Pierce and O'Connor originated the revival of preserved cartilage grafts prior to publication of this article.)

8. Peer, L. A.: *Cartilage Transplanted Beneath the Skin of the Chest in Man, Arch. Otolaryng.* 27: 42-58 (Jan.) 1938.

site of transplantation which healed promptly after drainage without loss of the graft. One must use care to remove all muscle, fascia and perichondrium from the graft before transplantation because the soft tissues of one individual when transplanted into another frequently give rise to considerable reaction. The cartilage cells embedded in the hyaline matrix do not come into contact with the surrounding host tissue to a great extent and hence cause very little irritation.

AUTOGENOUS RIB CARTILAGE

Fresh rib cartilage taken from the patient's chest is probably the most satisfactory tissue with which to repair skull defects. It retains its contour, is readily shaped as desired and is not subject to absorption. Like dermal grafts, fresh autogenous cartilage grafts become part of the living organism and remain as living tissue until the individual dies. Experimental studies at the Newark Eye and Ear Infirmary⁹ with sections of fresh autoplasmic cartilage grafts in human beings show that the cartilage retains its normal structure as living tissue after transplantation. This conclusion is based on

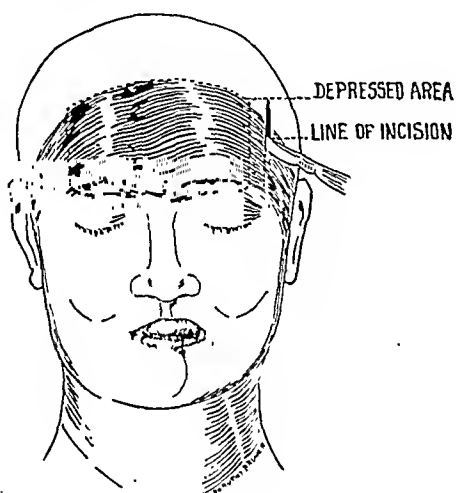


Fig. 3.—Deep depression in the frontal region.

microscopic examination of segments of costal cartilage buried beneath the chest skin of human beings and removed at intervals of six months, nine months, eleven months, seventeen months, eighteen months, two years, four and one-half years and six years.¹⁰

When repairing a large skull defect the surgeon may shorten the operative procedure by doing the operation in two or three stages. Thus in the forehead a rib cartilage segment, suitably shaped, may be inserted to fill out the brow during the first operation. At a later time additional cartilage may be inserted to elevate the depression above the reconstructed brow. Deep depressions may require two or three thicknesses of cartilage placed one on top of the other to obtain the desired elevation. The operator should use meticulous care to elevate only the skin and not carry his dissection into the brain substance. Epinephrine hydrochloride packs

during the operation and a firm dressing over the grafted area will control bleeding and lessen the danger of infection. Rib cartilage after transplantation without its perichondrium does not decrease or increase in size. It is, however, subject at times to distortions such

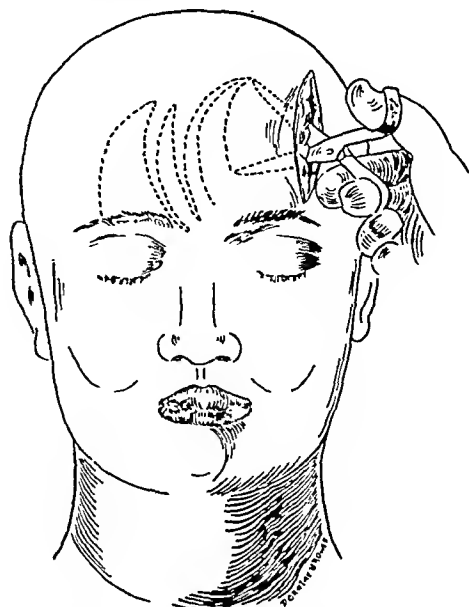


Fig. 4.—Releasing scalp skin over the depressed area.

as twisting or bending. In such cases one can easily insert a scalpel through a small incision and remove the projecting portion of cartilage. Living autogenous cartilage is very resistant to infection. One of my recent patients with an extensive depression in the

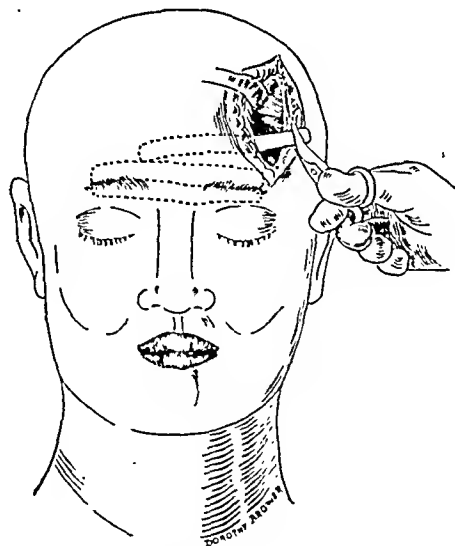


Fig. 5.—Insertion of rib cartilage.

frontal region contracted pneumonia following the insertion of a large autogenous cartilage graft. During the course of his pneumonia the cartilage graft became infected and after incision drained for three months. The cartilage, however, remained in place, and when the patient was last seen, two years after operation, the graft appeared to have the same gross bulk as when first inserted. On the basis of clinical experience and

9. Peer, L. A.: The Fate of Living and Dead Cartilage Transplanted in Humans, Surg., Gynec. & Obst. 68: 603-610 (March) 1939.

10. Dr. Warren Davis recently sent me stained sections of an autogenous costal cartilage graft buried with its perichondrium and removed thirteen years after transplantation. A small outer portion of this graft showed definite invasion by connective tissue. The larger bulk of the graft showed no invasion or absorption and the cartilage cells appeared normal. It is quite possible that the small area of cartilage invaded in Davis's graft was injured at the time of transplantation and the invading process represents an effort at removal and replacement of the devitalized cartilage.

from experimental evidence showing that autogenous cartilage survives after transplantation, I prefer this type of graft above all others that I have used.

BONE GRAFTS

A discussion of bone grafts will be omitted since they were not used in this series of cases. Carter,¹¹ Kazanjian,¹² Webster,¹³ Sheehan¹⁴ and many other excellent clinicians have used bone grafts successfully for various types of depressions.

A questionnaire sent to sixteen surgeons with considerable experience in this type of work revealed the following opinions: Seven men used only autogenous rib cartilage for cranial defects. Two men used only autogenous bone for cranial defects. Seven used autogenous bone for deep defects and autogenous cartilage for shallow defects. Five of the sixteen sometimes used preserved costal cartilage and two used dermal grafts for shallow defects.

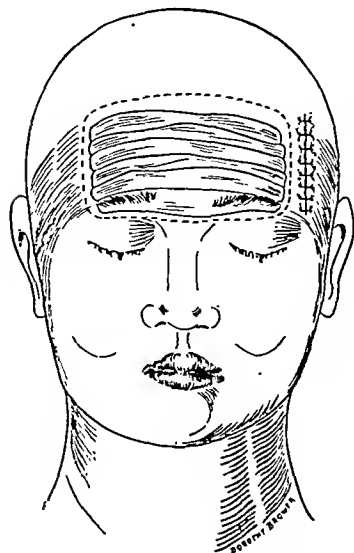


Fig. 6.—Position of rib cartilage, front view.

of the sixteen sometimes used preserved costal cartilage and two used dermal grafts for shallow defects.

SUMMARY

1. Dermal grafts, pickled cadaver cartilage and living autogenous cartilage were used in the repair in fifteen cases of skull depression.

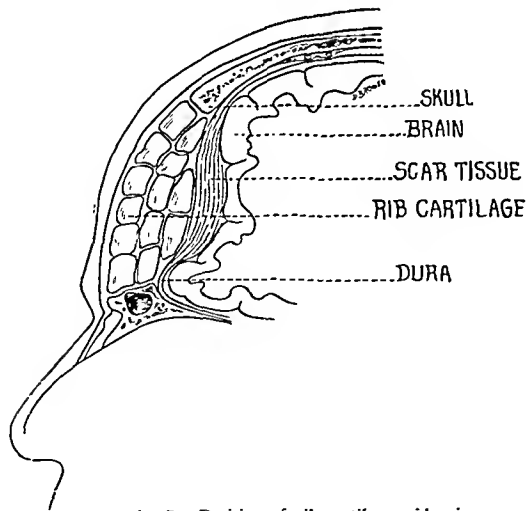


Fig. 7.—Position of rib cartilage, side view.

2. Dermal grafts are satisfactory for shallow depressions but tend to become infected more frequently than

11. Carter, W. W.: The Treatment of Fractures and Depressed Deformities, *Laryngoscope* 18: 683-691 (Sept.) 1908; The Ultimate Fate of Bone When Transplanted into the Nose, *Arch. Otolaryng.* 15: 563-573 (April) 1932.

12. Kazanjian, V. H., and Converse, J. M.: Reconstruction After Radical Operation for Osteomyelitis of the Frontal Bone, *Arch. Otolaryng.* 31: 94-112 (Jan.) 1940.

13. Webster, Jerome P.: Personal communication to the author.

14. Sheehan, J. Eastman: A Manual of Reporative Plastic Surgery, New York, Paul B. Hoeber, Inc., 1938, pp. 223-225.

cartilage grafts. When infection occurs the dermal graft will probably be lost.

3. Pickled cadaver cartilage is indicated with patients who will not consent to the removal of their own rib cartilage and with small children. It may also be used when the patients age or general condition contraindicates a long operation.

4. Living autogenous cartilage taken from the patient's chest is the most satisfactory tissue with which to repair skull depressions.

965 Broad Street.

Clinical Notes, Suggestions and New Instruments

ACUTE THROMBOPENIC PURPURA TREATED SUCCESSFULLY WITH SOLUTION OF PARATHYROID

DAVID B. LEVINE, M.D.
AND
HENRY MICHELSON, M.D.
PATERSON, N. J.

Thrombopenic purpura has been treated by a variety of agents, without consistent results. Blood transfusion and splenectomy¹ are the most favored procedures; other measures used include the administration of moccasin snake venom,² ascorbic acid, calcium, liver extract and occasionally other substances.³ In the case reported here all measures, including splenectomy, failed to alter the course of the disease; a spectacular remission followed administration of solution of parathyroid.

REVIEW OF REPORTED CASES

The literature contains detailed reports of five cases treated with large doses of solution of parathyroid in which there were four recoveries and one death.

In 1932 Lowenburg and Ginsburg⁴ reported the first case. A white boy aged 5 with purpura haemorrhagica was accidentally given large doses of solution of parathyroid. A total of 600 units was given in six days. Marked hypercalcemia developed, the serum calcium rising to a level of 19.6 mg. per hundred cubic centimeters. Concomitantly the hemorrhagic symptoms disappeared.

In 1936 the same authors presented a second case.⁵ A 7 year old white boy was unsuccessfully treated for essential thrombopenic purpura with moccasin snake venom. Solution of parathyroid was administered and hypercalcemia induced, the serum calcium reaching 18.8 mg. per hundred cubic centimeters. A total of 240 units of solution of parathyroid was given in four days. Immediate and spectacular clinical improvement followed, and a cause and effect relationship between the hypercalcemia and the apparent cures was suggested.

From the Surgical Service of Dr. William Spickers, Barnert Memorial Hospital.

1. Whipple, A. O.: Splenectomy as a Therapeutic Measure in Thrombopenic Purpura Haemorrhagica, *Surg., Gynec. & Obst.* 42: 329 (March) 1926. Brown, D. H., and Elliott, R. H. E.: The Results of Splenectomy in Thrombopenic Purpura: A Comparative Study of Ten Cases Treated by Conservative Methods, *J. A. M. A.* 107: 1781 (Nov. 28) 1936. Wintrobe, M. M.; Hanrahan, E. M., and Thomas, Caroline B.: Purpura Haemorrhagica, with Special Reference to Course and Treatment, *ibid.* 109: 1170 (Oct. 9) 1937.

2. Peck, S. M., and Rosenthal, Nathan: Effect of Moccasin Snake Venom (*Aricistodon Piscivorus*) in Hemorrhagic Conditions, *J. A. M. A.* 104: 1066 (March 30) 1935. Peck, S. M.; Rosenthal, Nathan, and Erf, L. A.: The Value of the Prognostic Venom Reaction in Thrombopenic Purpura, *ibid.* 106: 1783 (May 23) 1936.

3. Rosenthal, Nathan: The Course and Treatment of Thrombopenic Purpura, *J. A. M. A.* 112: 101 (Jan. 14) 1939.

4. Lowenburg, Harry, and Ginsburg, T. M.: Acute Hypercalcemia: Report of a Case, *J. A. M. A.* 99: 1166 (Oct. 1) 1932.

5. Lowenburg, Harry, and Ginsburg, T. M.: Induced Hypercalcemia: Its Possible Therapeutic Relation to Thrombopenic Purpura, *J. A. M. A.* 106: 1779 (May 23) 1936.

In 1937 Ainsworth, Edelman and Fried⁶ reported two additional cases of thrombocytopenic purpura in white girls aged 3 and 4 years. The purpura in one was apparently secondary to a preceding scarlet fever. In the other it followed closely on a diarrhea of unknown origin. Both were given solution of parathyroid, and prompt remission of all clinical symptoms and return of the normal hematologic picture ensued. The 3 year old child received a total of 140 units in three days; the 4 year old girl received a total of 200 units in four days. In both patients the serum calcium remained within normal limits during and after the parathyroid therapy.

In 1937 Mathewson and Cameron⁷ reported a single case of purpura in which solution of parathyroid failed to halt the progress of the disease. A white woman aged 26 with epistaxis, profuse menstrual flow and subcutaneous hemorrhages was given solution of parathyroid. A total of 300 units was administered in four days. Although the serum calcium did not rise above normal, the patient exhibited symptoms of parathyroid toxicity—nausea, vomiting and abdominal cramps. In spite of a rise in blood platelets from 100,000 to 290,000 per cubic millimeter the patient made no clinical response. Death resulted from multiple cerebral hemorrhages one week after the parathyroid therapy was begun. In this case the condition cannot be considered thrombopenic purpura in view of the relatively normal platelet count. This may have some bearing on the poor clinical response to solution of parathyroid.

Rosenthal⁸ in a recent review of thrombopenia stated that he had observed no beneficial effect on bleeding tendency or platelet count in five chronic and two acute cases, but he gave no further details. In each of the cases just summarized calcium was given together with solution of parathyroid.

REPORT OF CASE

P. L.,⁸ a white girl aged 12, began to menstruate at the age of 11. At first the periods occurred every four weeks and lasted seven days. Gradually the interval shortened to three weeks and the flow was prolonged to ten days. For a year, numerous purpuric spots were observed on her skin. On March 15, 1939, profuse vaginal bleeding with the passage of many clots began. She was admitted to the Barnert Memorial Hospital on April 2, still bleeding copiously. No antecedent history of infection was elicited. The family history was non-contributory. There were no siblings. During the three weeks immediately preceding hospitalization she had been given several injections of an anterior pituitary preparation without effect.

On admission the patient appeared well nourished, rather obese, very alert and intelligent and quite cooperative. The temperature was 101 F., pulse rate 120 and respiratory rate 25. There was a pronounced pallor of the skin, lips and conjunctivas. The teeth were well cared for and there was no bleeding from the gums. Examination of the heart, lungs and abdomen was negative. The spleen could not be palpated. On both arms were numerous purpuric areas at the site of the recent injections into the deltoid muscles.

Laboratory examination on admission revealed red blood cells 1,700,000, hemoglobin (Sahli) 25 per cent, platelets 25,000, white blood cells 16,400, polymorphonuclear neutrophils 82 per cent, lymphocytes 16 per cent, monocytes 2 per cent, bleeding time more than twenty minutes, no clot retraction at the end of twenty-four hours, tourniquet test markedly positive in one minute. A diagnosis of acute thrombopenic purpura was made.

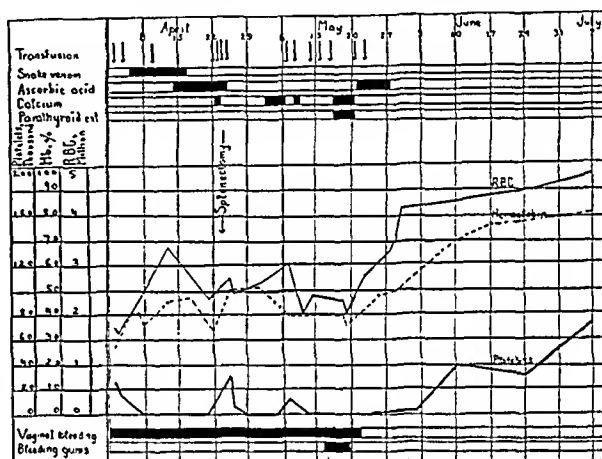
A blood transfusion of 250 cc. of citrated whole blood was given directly after admission. Fourteen transfusions were given within the next seven weeks. After two transfusions had produced no effect on the bleeding, the administration of moccasin snake venom was begun on April 6. The initial dose was 0.4 cc. of a 1:3,000 dilution. The dose was increased 0.1 cc.

daily to a maximum of 1 cc. Eleven injections were given and then discontinued, as no improvement in the clinical or laboratory evidence occurred. The platelet count fell to zero.

Ascorbic acid was begun on April 15 and continued for eleven days with no discernible improvement.

Splenectomy was performed on April 24. The operation was uneventful and postoperative recovery rapid, but vaginal bleeding continued. The platelets rose to 30,000 per cubic millimeter after splenectomy but within a few days again disappeared from the blood. A bone marrow puncture on May 7 showed the presence of many megakaryocytes without much maturation. On this date the appearance of abdominal pain and nausea suggested the onset of intra-abdominal bleeding. The patient failed steadily. There was a noticeable loss of weight. The appetite was poor and she grew progressively weaker. On May 15, bleeding from the gums began and the patient appeared moribund.

May 17, 50 units of solution of parathyroid was given subcutaneously, and May 18 100 units with no reaction. May 19 the dose of 100 units was repeated. Several hours later she complained of abdominal pain, headache and generalized soreness throughout the body. May 20 the last dose of solution of parathyroid, 150 units, was given. She became extremely irri-



Summary of hemoglobin, erythrocyte and platelet determinations and the treatment given.

table, cried hysterically and complained of numbness in both lower extremities. Nausea and vomiting were present throughout the day. The pulse became weak and occasionally irregular. Blood and clots were passed from the vagina, but the gingival bleeding had stopped.

The following morning, May 21, the patient was still disturbed and almost irrational at times and continued to complain of numbness of the legs. In the evening she seemed transformed—cheerful and bright and more interested in her surroundings. There was no bleeding after this day. The appetite returned, and on May 25 the patient was out of bed and convalescent.

The serum calcium levels were 10.2 mg. per hundred cubic centimeters immediately before the first injection of solution of parathyroid, 9.5 mg. immediately after the last injection, and 9.8 mg. one week later. Ten cc. of calcium gluconate was given intravenously with each injection of solution of parathyroid. Similar doses of calcium had been given previously without effect on the bleeding.

The patient's subsequent course was uneventful. She was discharged from the hospital June 7. No bleeding had occurred since May 21, the day after the last injection of solution of parathyroid. The hemoglobin had risen to 60 per cent and the erythrocytes to 3,800,000. Platelets were still absent from the blood stream.

She has been followed for eleven months with no sign of recurrence. Menstrual periods have recurred at intervals of

6. Ainsworth, M. L.; Edelman, S. D., and Fried, R. I.: Thrombopenic Purpura Haemorrhagica: Two Cases Treated with Parathyroid Hormone and Calcium Gluconate. *J. Pediatr.* 11: 559 (Oct.) 1937.

7. Mathewson, F. A. L., and Cameron, A. T.: An Apparent Instance of Parathormone Inactivity. *Canad. M. A. J.* 36: 141 (Feb.) 1937.

8. This patient was seen through the courtesy of Dr. M. S. Joelson.

from twenty-eight to thirty days, lasting four or five days each, with a normal amount of flow. The hemoglobin and erythrocytes are slowly approaching normal levels, but two months after discharge the platelets numbered only 75,000.

In the chart are summarized the hemoglobin, erythrocyte and platelet determinations and the treatment given. In the table the remaining blood data are summarized.

COMMENT

Although thrombopenic purpura often exhibits periods of exacerbation and spontaneous remission, we do not believe the remission in this case to have been spontaneous or coincidental. All measures used including splenectomy failed to arrest the bleeding. Repeated transfusions were insufficient to sustain the patient. The condition was grave. The sudden and sustained improvement which followed the administration of solution of parathyroid seems to indicate the specificity of the agent in this case.

The exact nature of the action of parathyroid in these cases awaits clarification. The administration of large doses of solution of parathyroid alters the state of equilibrium of the calcium of the body. The participation of calcium ions in blood clotting by direct activation of prothrombin has long been established.⁹ According to Peters and Van Slyke,¹⁰ from 40 to 50 per cent of the normal serum calcium is held in solution through the action of parathyroid hormone. This is the physiologically active fraction of the serum calcium. Theoretically the parathyroid may exert its effect by increasing the solubility of

Summary of Blood Tests

Date	White Blood Cells	Poly-morpho-nuclears	Lym-pho-cytes	Mono-cytes	Baso-phils	Eosino-phils	Bleeding Time
4-2-39	16,400	82%	16%	2%	More than 20 minutes
4-8-39	7,200	64%	30%	5%	1%	...	
4-25-39	8,100	62%	30%	5%	...	2%	
5-1-39	More than 20 minutes
5-26-39	18 minutes
6-1-39	9,200	34%	63%	3%	
6-17-39	8,800	49%	40%	5%	...	6%	

calcium and phosphate in serum and body fluids. Hastings, Murray and Sendroy¹¹ demonstrated that the addition of solution of parathyroid enables serum to dissolve more calcium.

Lowenburg and Ginsburg⁵ suggested that the hypercalcemia observed in both their cases might have brought about their apparent cures. However, in none of the subsequent cases, including our own, is the presence of hypercalcemia reported. It would seem more likely that some qualitative change occurring in the physicochemical state of the blood calcium rather than a purely quantitative increase is responsible. Although the blood calcium remains at its normal level, it may be made more available for the clotting cycle by the action of the parathyroid hormone.

SUMMARY

1. A successful instance of the use of solution of parathyroid in thrombopenic purpura is added to the four other successful cases and one unsuccessful case previously reported.
2. Our patient is older than those mentioned in previous reports, with the exception of the patient described by Mathewson and Cameron, for whom solution of parathyroid was ineffective.
3. A total of 400 units of solution of parathyroid in four days was given after splenectomy had failed.
4. Dramatic recovery occurred of an apparently moribund patient.

647 Broadway—557 Broadway.

9. Howell, W. H.: A Textbook of Physiology, ed. 7, Philadelphia, W. B. Saunders Company, 1918, p. 459.
10. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 1, pp. 810-820.
11. Hastings, A. B.; Murray, C. D., and Sendroy, Julius, Jr.: Studies of the Solubility of Calcium Salts: I. The Solubility of Calcium Carbonate in Salt Solutions and Biological Fluids, J. Biol. Chem. 71: 23 (Feb.) 1927.

HEMATURIA FROM SULFATHIAZOLE THERAPY
IN PNEUMONIA

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The tendency of sulfapyridine to form urinary crystals resulting in hematuria and even obstruction is by this time well known. Gross, Cooper and Scott¹ have collected from the literature thirty-six cases of gross hematuria, with seven in which uroliths were specifically mentioned, complete bilateral ureteral block being disclosed at autopsy in one instance.² Plummer and McLellan³ have reported two cases of unilateral calculus formation, one of which was fatal. Arnett, Shoup and Henry⁴ have reported a case of bilateral ureteral obstruction with recovery. The fact that similar complications can arise in the course of sulfathiazole therapy is now beginning to be recognized. Gross, Cooper and Scott¹ have demonstrated concretions in the kidneys of rats receiving sulfathiazole, and Pepper and Horack⁵ reported the death of a 77 year old pneumonia patient who developed hematuria and oliguria while on sulfathiazole therapy. At autopsy the kidneys were found to be large and soft and their collecting tubules were dilated and contained crystalline material. In the case here reported severe hematuria and lumbar pain were present but the patient recovered.

REPORT OF CASE

L. E., a woman aged 72, residing in Christ Church Hospital, a home for aged women, had been receiving digitalis for auricular fibrillation, which began in February 1940 incident to hypertensive cardiovascular disease of many years' standing. On April 13, 1940, pain developed in the chest. On the following day early signs of pneumonia were noted at the base of the left lung, the leukocyte count was 13,700, rusty sputum appeared and the temperature was 99.6 F. On April 15 the signs of pneumonia became unequivocal, and at 8 a. m. 2 Gm. (30 grains) of sulfathiazole was given, followed every four hours by half this amount of the drug and an equal quantity of sodium bicarbonate. The temperature varied between normal and 100 F., the respiratory rate was 28 and the patient's condition remained satisfactory. The appearance of the urine was noteworthy; previous to sulfathiazole medication it had been clear, acid in reaction and free from sediment, with only an occasional hyaline cast and a few leukocytes, and when it was boiled gave a heavy cloud of albumin. On April 16 it was acid and had a muddy appearance with abundant brownish sediment which separated readily on centrifugation. The sediment proved on microscopic examination to be composed almost entirely of the dumb-bell, rosette and chestnut-burr shaped crystals so frequently found during the course of sulfathiazole therapy. Blood culture gave negative results. The sputum contained micrococci of the catarrhalis group, staphylococci and Streptococcus viridans but no pneumococci in smear or on culture. The blood sulfathiazole was 6 mg. per hundred cubic centimeters.

On April 17, after a total of 14 Gm. of sulfathiazole had been taken in forty-eight hours, the urine became extremely bloody and the patient complained of intense pain in the lumbar region. Deep percussion over the left kidney was painful. The urinary output, which had been 960 cc. on the previous day, was 570 cc. plus an unknown quantity which was lost with defecation. The blood pressure was 150/100. Sulfathiazole was stopped and 900 cc. of 5 per cent dextrose in physiologic solution of sodium chloride was administered by vein. The sulfathiazole level of the blood at this time was 7 mg. per hundred cubic centimeters.⁶ On the following day the lumbar

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2. Tsao, Y. T.; McCracken, M. E.; Chen, Ji; Kuo, P. T., and Dale, C. L.: Renal Complications in Sulfapyridine Therapy, J. A. M. A. 113: 1316 (Sept. 30) 1939.
3. Plummer, Norman, and McLellan, Frederick: The Production of Sulfapyridine: Renal Calculi in Man, J. A. M. A. 114: 943 (March 16) 1940.
4. Arnett, J. H.; Shoup, G. D., and Henry, N., to be published.
5. Pepper, D. S., and Horack, H. M.: Crystalline Concretions in the Renal Tubules Following Sulfathiazole Therapy: Widely Patent Foramen Ovale in a Patient Aged 77, Am. J. M. Sc. 199: 674 (May) 1940.
6. The sputum, blood culture and blood chemistry work here reported was done by Dr. William P. Belk, director of the Pathological Laboratory of the Episcopal Hospital.

pain had subsided, the urine was slightly less bloody, although it was still full of blood cells and crystals, and the patient's general condition was improved. Convalescence continued slowly, the characteristic crystals disappearing from the urine on April 20 and the erythrocytes on April 22, on which date the blood urea nitrogen and blood count were normal. Nausea and occasionally vomiting were annoying before, during and after the period of disease and were apparently not affected by diet or the administration or discontinuance of digitalis, sulfathiazole or other therapeutic measures. Throughout the course of the disease, however, this complication interfered somewhat with the free ingestion of fluids. With this exception convalescence was satisfactory though slow, the chest being free from abnormal signs and the patient up much of the day by the middle of May.

COMMENT

It is the currently accepted belief that sulfathiazole, like sulfapyridine, may produce hematuria mechanically through the irritation caused by the crystals precipitated in the renal tubules and pelvis. No doubt the fact that in the present case, because of vomiting, it was impossible to maintain a sufficiently high fluid intake to prevent such precipitation was an important factor in causing the hematuria. The fact that such a complication may arise should not discourage the medical profession from using sulfathiazole, which is probably less toxic and more efficacious in cases of pneumonia than sulfapyridine. In 200 cases of pneumonia, half of which were treated by the former and half by the latter drug, Flippin, Schwartz and Rose⁷ report only one case of gross hematuria, and this occurred in the sulfapyridine group, while the mortality in the sulfathiazole group was lower by 3 per cent and vomiting was much less frequent. The point that should be emphasized is the importance of maintaining a sufficiently high fluid intake to prevent massive crystal formation. The fluid intake and urinary output should receive the watchful attention of the physician, and the urine should be examined at least daily for crystals and blood. If the intake can be kept in excess of 3,000 cc. and the output at 1,500 cc. or more a day, and if the drug is immediately discontinued and intravenous fluids are administered with the first appearance of lumbar pain or bloody urine, the dangers from renal complications will be reduced to a minimum.

2116 Pine Street.

GRANULOMATOUS TUMOR FOLLOWING INTRA-
MAMMARY INJECTION OF COLLOIDAL
THORIUM DIOXIDE

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Recent studies in the roentgenographic demonstration of tumors of the breast after injection of the ducts with an opaque medium have aroused considerable enthusiasm. It is not generally appreciated, however, that this diagnostic procedure may produce untoward reactions of considerable moment.

Mammography was first suggested by Ries,¹ of Chicago, who in 1930 reported one case in which iodized poppyseed oil was injected intraductally. This was unfortunately followed by abscess formation. No other studies of similar nature were made by any one until 1937, when Hicken and his associates² reported the use of this method in fifty-six cases, using colloidal thorium dioxide in most instances. Hicken's study suggested that by this method it might be possible to differentiate localized from infiltrating growths, solid from cystic tumors, and simple retention cysts from cystic degeneration of the breast. He felt that it was especially valuable in determining the location, number and size of papillomatous tumors. The contraindications

to injection were given as frankly malignant growths and acute infections.

Of the various mediums used—colloidal thorium dioxide, lipoiodine, hippuran, diodrast, bismuth oxychloride, sodium iodide (15 per cent) and air—colloidal thorium dioxide appeared



Fig. 1.—Low power magnification. Masses of cells with cytoplasmic inclusions of granular deposits.

to be the least irritating and most suitable because its fluidity permitted the filling of the smallest ducts and yet was of sufficient density to cast a satisfactory shadow. Hicken and his associates felt there was little danger in using colloidal thorium



Fig. 2.—High power magnification. Histiocytes are loaded with the foreign substance (colloidal thorium dioxide), none of which is seen in the interstitial tissue.

dioxide because the injection was intraductal and not intravenous, the quantity injected was small, the mammary ductal system had low absorptive powers, and the substance used (thorotrast, a stabilized 25 per cent solution of colloidal thorium dioxide) could be removed from the ducts by lavage with phys-

7. Flippin, H. F.; Schwartz, Leon, and Rose, S. B.: The Comparative Effectiveness and Toxicity of Sulfathiazole and Sulfapyridine in Pneumococcal Pneumonia, *Ann. Int. Med.* 13: 2038 (May) 1940.

From the Department of Surgery, University of Illinois College of Medicine, and the Mount Sinai Hospital.

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2. Hicken, N. F.: Mammography: The Roentgenographic Diagnosis of Breast Tumors by Means of Contrast Media, *Surg., Gynec. & Obst.* 64: 593-603 (March) 1937. Hicken, N. F.; Best, R. R.; Moon, C. F. and Harris, T. T.: The Preoperative Visualization of Breast Tumors, *I. A. M. A.* 108: 864-867 (March 13) 1937. Hicken, N. F.; Best, R. R., and Tallman, J. P.: Mammographic Recognition of Intra-cystic Papilloma of the Breast, *Am. J. Surg.* 36: 611-617 (June) 1937.

iologic solution of sodium chloride followed by evacuation with a breast pump. In 350 injections Hicken had only two mishaps, each consisting of multiple abscesses following injections in the presence of acute mastitis.

Colloidal thorium dioxide is a dangerous substance, dangerous because of its most important characteristic, radioactivity. A recent editorial³ points out the hazards of using this substance and calls attention to the fact that the disintegration products of thorium emit alpha rays more penetrating than those of the radium series and that this ray is about 10,000 times as toxic to tissues as the gamma ray which is used therapeutically. Small quantities of thorium dioxide will produce marked local tissue changes. Selbie⁴ injected 1.3 cc. of this substance into the flank of each of sixty rats. He found that the thorium dioxide had remained localized in firm yellow nodules, which on microscopic study showed many macrophages that had ingested the drug in the form of highly refractile yellow granules. After fifteen months definite tumors were found in fourteen of the sixty rats, each such tumor being a spindle cell sarcoma. Two of the disintegration products of thorium are mesothorium and radiothorium, the two main constituents of luminous paints, which produced fatal poisoning in dial painters as the result of ingestion.

Recent reports by several observers (using Hicken's technic) have indicated the frequency of untoward results following the use of thorium dioxide. Romano and McFetridge⁵ studied twenty-five cases in twenty-three of which some surgical procedure was required. In thirteen of the twenty-three cases the mammographic diagnosis agreed with the clinical and pathologic diagnoses. In the other cases the diagnosis was not clear or was actually incorrect. In four cases the injections gave rise to foreign body reactions, three of which were very severe; in two of the three cases amputation of the breast would have been necessary because of the reaction had it not already been planned for the primary lesion. In an experimental study Romano and McFetridge noted foreign body reactions in 50 per cent of the animals used, reactions similar to those seen in women. The reaction was of the foreign body type with periductal infiltration with leukocytes, large phagocytic cells filled with refractile granules of the injected substance, and in late cases actual necrosis. Romano and McFetridge concluded that the method as now employed does not contribute diagnostic aid of sufficient value to warrant risks of serious reactions.

Sowers and Masson⁶ record a case of extensive fat necrosis requiring mastectomy which followed injection of colloidal thorium dioxide.

Ries and Mesirow⁷ report that three patients suffered considerable pain and tenderness of the breast following injections of colloidal thorium dioxide. Follow-up roentgenograms showed the substance in the lactiferous ducts for as long a time as ten months after the original injection. Two patients required operation for relief. The retained thorium dioxide caused a marked foreign body reaction—macrophage infiltration, giant cell formation, connective tissue hyalinization and necrosis.

In my own case, a similar reaction was produced:

REPORT OF CASE

F. S., a white woman aged 40, married, had an intraductal injection of colloidal thorium dioxide in another hospital thirteen months prior to admission to the Mount Sinai Hospital. Six months after the injection she first noted a small tender mass just inferior and lateral to the left nipple. This gradually increased in size, and when she was first seen, thirteen months after the injection, a small firm sensitive mass was found, about 1.5 cm. in diameter. There had been no discharge from the nipple, and no axillary glands were palpable.

The mass was excised; grossly, it was firm and yellow-brown and appeared to be sharply circumscribed. It measured 15 by 10 mm. Microscopic examination disclosed large masses of oval and polygonal cells with small dark nuclei surrounding areas of hyalinized connective tissue. The cytoplasm was loaded with a granular material having a glistening appearance. This material was present mainly within the cells, although some was present in the interstitial tissue. Around these deposits of foreign material were occasional small islands of mammary parenchyma in groups of ducts surrounded by cells loaded with the substance just mentioned. Accumulations of large masses of endothelial cells and endothelial giant cells were noted in one area. The pathologist reported an isolated area with a granuloma; in most areas there were the manifestations of a very intensive process of phagocytosis by histiocytes of a foreign substance.⁸

1853 West Polk Street.

Special Clinical Article

THE TOXIC MANIFESTATIONS OF SULFANILAMIDE AND ITS DERIVATIVES

WITH REFERENCE TO THEIR IMPORTANCE IN
THE COURSE OF THERAPY

CLINICAL LECTURE AT NEW YORK SESSION

PERRIN H. LONG, M.D.

JAMES W. HAVILAND, M.D.

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AND

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BALTIMORE

It has become increasingly evident as time goes on that physicians often hesitate to use sulfanilamide or its derivatives because of a fear of the toxic manifestations of these drugs, while patients, because of their lack of appreciation of the possible toxic manifestations of this group of drugs, demand that the drugs be administered to them. These attitudes have at times brought about a somewhat peculiar situation.

It has seemed to us that physicians have been "oversold" on the dangers connected with the use of sulfanilamide and its derivatives and that these drugs can be used with greater impunity than has hitherto been considered possible. It is for this reason that we have carefully analyzed the incidence and types of toxic reactions occurring in hospitalized adults, 1,000 of whom were treated with sulfanilamide, 297 with sulfapyridine and 291 with sulfathiazole in the Johns Hopkins Hospital during the past few years. The results of this analysis are shown in the accompanying table.

It is obvious that certain deductions can be made from this group of patients in respect to the frequency and severity of the toxic manifestations of sulfanilamide or its derivatives, and we think that by a careful study of the clinical histories of these patients certain general

3. Potential Hazards of the Diagnostic Use of Thorium Dioxide Sol, editorial, J. A. M. A. 108: 1656 (May 8) 1937.

4. Selbie, F. R.: Experimental Production of Sarcoma with Thorotrast, Lancet 2: 847-848 (Oct. 10) 1936.

5. Romano, S. A., and McFetridge, E. M.: The Limitations and Dangers of Mammography by Contrast Mediums, J. A. M. A. 110: 1905 (June 4) 1938.

6. Sowers, B. F., and Masson, J. C.: Mastitis Following Use of Thorium Dioxide: Report of Case, Proc. Staff Meet., Mayo Clin. 12: 529 (Aug. 25) 1937.

7. Ries, R. A., and Mesirow, S. D.: Studies in the Evaluation of Mammography, J. A. M. A. 110: 1900-1905 (June 4) 1938.

8. Pathologic report by Dr. Israel Davidsohn.

Supported by a grant from the Chemical Foundation, Inc., New York. From the Medical Clinic, Johns Hopkins Hospital, and the Department of Medicine, Johns Hopkins University School of Medicine.

Dr. Edwards is Fellow in Medicine, E. R. Squibb & Sons, and Dr. Bliss is Fellow in Medicine, Calco Chemical Division of the American Cyanamid Company.

Read in the Symposium on Chemotherapy, General Scientific Meeting, at the Ninety-First Annual Session of the American Medical Association, New York, June 11, 1940.

conclusions can be drawn regarding the care of patients who are receiving these drugs.

In the first place it is to be noted that nausea and vomiting constitute a problem only as far as sulfapyridine therapy is concerned. We have noted that the more highly integrated the patient is, the greater the chance that nausea and vomiting will occur in the course of therapy with sulfapyridine. In our Negro patients and in children, nausea and vomiting have caused little if any difficulty in the maintenance of therapy, but in the private wards this toxic manifestation has occasionally been a problem of grave importance. When severe nausea and vomiting occur, the fluid intake should be kept at a high level and sodium chloride administered either by mouth or parenterally in order to prevent dehydration and hypochloremia from developing.

Although adequate statistics are not available, it has seemed to us that dizziness is more common in the course of sulfanilamide therapy than when sulfapyridine or sulfathiazole is being used. The recognition that dizziness may occur is of great importance, especially with respect to patients who drive automobiles, perform heavy or light mechanical work, pilot airplanes or conduct other types of vehicles. All ambulatory patients who are receiving these drugs should be warned of the consequences that may arise from attacks of dizziness.

True toxic psychoses due to the drug are fortunately rare, but they may take almost any form; if a manic type of psychosis is present the patient should be carefully watched lest harm come to him. In general it is always best to stop the drug when such toxic manifestations arise. Neuritis, either peripheral or central, is fortunately very rare in the course of therapy with sulfanilamide, sulfapyridine or sulfathiazole, but if evidence of this toxic manifestation is noted the drug should be immediately stopped.

Cyanosis, either mild or severe, is very common in the course of treatment with sulfanilamide but is of little importance except possibly in older persons suffering from emphysema or any type of cardiac disease. In the course of treating lobar pneumonia with sulfapyridine we have never noticed that this drug contributed significantly to the cyanosis already present, and indeed we have repeatedly observed that successful chemotherapy was attended by a marked decrease in the degree of cyanosis present. Our experience with sulfathiazole leads us to believe that this drug produces minimal degrees of cyanosis.

Acidosis has not been reported in the course of sulfapyridine or sulfathiazole therapy, and in our experience it has practically been eliminated as a toxic reaction of sulfanilamide therapy by the concurrent use of sodium bicarbonate with each administration of sulfanilamide. We have never seen a clinical example of alkalosis produced by the administration of sodium bicarbonate in the course of sulfanilamide therapy.

Drug fever is an extremely common toxic manifestation in the course of sulfanilamide or sulfathiazole therapy. It may occur at any time from the first to the thirtieth day of treatment, but it is most commonly seen between the fifth and ninth day of treatment. Drug fever may be of three clinical types: a hectic remitting fever accompanied by chills of great severity, a steadily mounting fever and a low continuous fever. We are frequently asked to distinguish between the fever

produced by the drug and the fever produced by infection. Since drug fever occurs most commonly from the fifth to the ninth day and since one expects the temperature of adequately treated patients to be normal by the third day, the appearance of fever, when all clinical signs are pointing toward a favorable termination of the disease, should immediately lead one to suspect that the rise in temperature is due to the drug and not to a recrudescence of the infection. Another factor of considerable importance is that when drug fever appears the patient begins to feel bad and almost always complains of headache and generalized malaise.

Simple drug fever in itself is probably not a dangerous toxic manifestation, but it has always seemed best to us to discontinue the drug if it makes its appearance. When the drug is stopped and fluids are vigorously forced, the temperature should return to normal within twelve to seventy-two hours, depending on the rapidity with which the drug is eliminated from the body. The slower the elimination of the drug, the more prolonged will be the fever.

Drug rashes are common in the course of sulfanilamide and sulfathiazole therapy but do not occur very often when sulfapyridine is being used. They may take any form, and we have seen erysipeloid, scarlatiniform, morbilliform, purpuric, erythema multiforme, papular, vesicular, pustular and nodular eruptions. In severe instances (especially if the drug is continued) the rash may progress to an exfoliating dermatitis. Rashes may occur at any time from the first to the thirtieth day of therapy. In a certain number of instances photosensitization of the skin seems to play a role in the production of the rash. For this reason patients who are receiving treatment with sulfanilamide or one of its derivatives should stay out of the sun until at least three days after cessation of therapy. A curious idea has recently become prevalent in this country, namely that patients who have received sulfanilamide or one of its derivatives during the winter should keep out of the sun during the summer. There is absolutely no foundation in fact for this rumor.

Hepatitis characterized by jaundice without anemia and a definite impairment of liver function has occurred in 0.6 per cent of patients who have been treated with sulfanilamide. This toxic reaction may occur early or late in the course of therapy. It has been noted that occasionally it accompanies dermatitis exfoliativa. In our experience the prognosis has been excellent if the drug is stopped immediately and fluids are forced, and as far as we know there has been no permanent impairment of liver function following recovery from this toxic reaction of sulfanilamide therapy. The occurrence of hepatitis in the course of sulfapyridine therapy has been reported, but we have not seen it in our series of patients treated with this drug. As far as we know, hepatitis has not occurred in the course of sulfathiazole therapy, although it is to be expected.

Leukopenia with granulocytopenia may occur early or late in the course of therapy with sulfanilamide or its derivatives. In adults this toxic manifestation is relatively uncommon. We have noted a sharp drop in the leukocytes following a single dose of sulfanilamide in certain cases, and we have also noted that granulocytopenia may not occur until the sixtieth or seventieth day of treatment. Hence one must always be on the lookout for this type of toxic manifestation.

It has been considered best to stop therapy with the drug if this toxic manifestation makes its appearance, but it must also be remembered that as far as we know there have not been any deaths reported from disturbances of the white cells during the first twelve days of therapy with any of these drugs.

Acute agranulocytosis is a rare complication of therapy with sulfanilamide and sulfapyridine and has not yet been reported in the course of therapy with sulfathiazole. This complication has in our experience occurred on the fourteenth or on a subsequent day of treatment with these drugs. The most common time for its appearance is between the seventeenth and the twenty-fifth day, although it may appear as late as the fortieth day of treatment. For this reason it is very

of sulfapyridine treatment and has not been reported as yet in patients who are receiving sulfathiazole. In contradistinction to acute hemolytic anemia, it seems to occur as frequently in white as it does in Negro patients. These mild anemias should not be considered as alarming toxic manifestations, as they generally disappear when the drug is stopped and may be combated by the administration of 0.6 Gm. of ferrous sulfate daily. In patients suffering from chronic osteomyelitis or other diseases in which it may be desirable to prescribe sulfanilamide over long periods of time, occasional transfusions will help to control these mild hemolytic anemias.

Acute hemolytic anemias occurred in 1.8 per cent of our adult patients who were treated with sulfanilamide

Manifestations of Drug Toxicity Noted in Hospitalized Adults; 1,000 Treated with Sulfanilamide, 297 Treated with Sulfapyridine and 271 Treated with Sulfathiazole

Reaction	Sulfanilamide	Sulfapyridine	Sulfathiazole
Nausea, vomiting.....	Fairly common	Frequent	Uncommon
Dizziness.....	Common	Common	Uncommon
Psychoses *.....	0.6%, occur early	0.3%, occur early	Not reported as yet
Neuritis †.....	Very rare	Not reported	Not reported
Cyanosis.....	Very common, early and late	Faint, common, early and late	Uncommon
Acidosis *.....	1.9%, occurs at any time, rare if soda is used	Not reported	Not reported
Fever *.....	10%, generally 5th to 9th day, may occur 1st to 30th day	4%, generally 5th to 9th day, may occur 1st to 30th day	10%, generally 5th to 9th day
Rash *.....	1.0%, may take any form, generally 5th to 9th day, may occur 1st to 30th day	2%, may take any form, 5th to 9th day, may occur 1st to 30th day	5%, nodular type common, may take any form, 5th to 9th day
Hepatitis †.....	0.6%, early or late	Not seen, but reported	Not reported
Leukopenia with granulocytopenia †.....	0.3%, early or late	0.6%, early or late	1.6%, early or late
Acute agranulocytosis †.....	0.1%, occurs 14th to 40th day, common 17th to 25th day	0.3%, occurs 14th to 40th day, common 17th to 25th day	Not reported
Mild hemolytic anemia.....	3%, early and late	Rare	Not reported
Acute hemolytic anemia †.....	1.8%, occurs 1st to 5th day	0.6%, occurs 1st to 5th day	Not reported
Hematuria *.....	Not reported	8%, generally early	2.6%, generally early
Anuria with azotemia †.....	Not reported	0.3%, generally 1st 10 days	0.7%, generally 1st 10 days
Hyperleukocytosis *.....	Generally in presence of acute hemolytic anemia	Generally in presence of acute hemolytic anemia	Not reported
Injection of scleras and conjunctivas *...	Not reported	Not reported	4%, may occur with rash and fever, 5th to 9th day
Purpura haemorrhagica †.....	Not seen, but reported	Not seen, but reported	Not reported
Ocular and auditory disturbances *.....	Rare	Rare	Not reported
Jaundice †.....	With acute hemolytic anemia or hepatitis	With acute hemolytic anemia or hepatitis	Not reported
Painful joints *.....	Reported	Not reported	Reported with rash, etc.
Stomatitis †.....	Rare	Not reported	Not reported
Gastrointestinal tract disturbances *.....	Bleeding rare, diarrhea uncommon	Rare	Not reported

* Best to stop drug and force fluids.

† Imperative to stop drug and force fluids.

important to check the white blood cell count at daily intervals on and after the twelfth day of treatment with sulfanilamide or its derivatives. If the white blood cell count drops and the polymorphonuclear leukocytes are decreased, it probably means the beginning of acute agranulocytosis. The drug should be stopped and fluids vigorously forced in order that the drug may be eliminated from the body as quickly as possible. Outside of this measure, it is probably unwise to attempt other therapeutic procedures designed to combat the agranulocytosis, except that we believe that it is a good plan to use transfusions when the hemoglobin content falls below 70 per cent. In our experience the prognosis of agranulocytosis occurring in the course of therapy with sulfanilamide and its derivatives is good if the toxic reaction is recognized in its inception.

Mild, slowly developing hemolytic anemia, in which the hemoglobin content drops 20 per cent or more during the first ten days of treatment, has occurred in 3 per cent of the adult patients treated with sulfanilamide. This toxic manifestation is rare in the course

and in 0.6 per cent of those who received sulfapyridine. It has not yet been reported in the course of sulfathiazole therapy. In practically all instances it makes its appearance in the first five days of treatment with these drugs and can almost always be recognized clinically by the sudden development of pallor of the mucous membranes of the mouth and conjunctivas. Mild jaundice almost invariably accompanies this toxic manifestation of drug therapy and is especially noticeable in the scleras. In very acute fulminating cases, hemoglobinemia and hemoglobinuria may be present. Urobilin is consistently found in the urine. We have seen patients whose hemoglobin content has dropped as much as 70 per cent within twenty-four hours when this toxic manifestation has made its appearance.

If possible, it is always best to stop the drug when an acute hemolytic anemia is present. However, in certain cases of severe involvement in which the continuance of therapy has been a life-saving procedure, multiple transfusions have been used in order to maintain the red blood cell count until the critical period

of the illness has passed and it is possible to stop the drug. In most instances it has been necessary to administer one or more transfusions to combat this toxic manifestation.

Hematuria has not been reported in the course of therapy with sulfanilamide but is quite frequent when sulfapyridine or sulfathiazole is being used. Hematuria may be either microscopic or gross and may be a precursor of severe renal insufficiency. We have generally considered it best to stop the drug if hematuria makes its appearance, but in several instances we have observed patients in whom hematuria developed and in whom the continuance of therapy did not result in any grave kidney lesion.

Anuria with concurrent azotemia has not been reported in the course of sulfanilamide therapy but has been noted in the course of treatment with sulfapyridine or sulfathiazole. The anuria may be due to a true toxic injury of the tubules of the kidney, probably similar to that seen in mercury bichloride poisoning, or it may be due to the deposition of acetylsulfapyridine or acetylsulfathiazole crystals in the kidney tubules, and on occasion to the blocking of the renal pelvis and ureters by calculi composed of acetylsulfapyridine or acetylsulfathiazole.

If anuria makes its appearance, fluids should be forced by mouth and by the parenteral route. If vomiting is present, sodium chloride should be given by mouth or in the form of physiologic solution of sodium chloride by the parenteral route, because it is important to prevent hypochloremia from developing. If the anuria persists for more than twenty-four hours, the ureters should be carefully catheterized, and if obstruction is found an attempt should be made to wash out the ureters and renal pelvis gently with warm physiologic solution of sodium chloride in order to remove the renal calculi. If obstruction is not present, fluids should be forced, and in our experience all such patients have eventually recovered from this toxic manifestation of the drug.

Hyperleukocytosis has been seen in this series of cases only when acute hemolytic anemia has been present. We have noticed total white blood cell counts ranging as high as 90,000 cells in the presence of acute hemolytic anemia. These very high white blood cell counts probably represent an abnormal response of the bone marrow to a hurried call made on it by the rapidly developing anemia. In this connection one should always remember that many nucleated red blood cells are being thrown into the circulation and that an allowance should be made for this fact in calculating the total white blood cell count.

Purpura haemorrhagica has not been seen in any of our cases but it has been reported as occurring in the course of therapy with sulfanilamide and sulfapyridine. If this toxic manifestation is noted, the drug should be stopped and fluids forced.

An injection of the scleras and conjunctivas, which may be so severe as to resemble "pink eye," has been noted quite frequently in the course of sulfathiazole therapy. It generally occurs between the fifth and the ninth day of treatment with this drug, and its appearance is often heralded by burning and smarting of the eyes.

Other ocular and auditory disturbances, such as visual and auditory hallucinations and changes in visual and auditory acuity, have been noted in the course of sulfanilamide therapy, but they are rare.

Painful joints have been reported in the course of sulfanilamide therapy, and we have noted that several patients who have received sulfathiazole have had exquisitely tender, swollen joints. This toxic manifestation may be puzzling when the patient is suffering from gonorrhea because of its resemblance to acute gonorrheal arthritis.

Stomatitis has been encountered rarely in the course of sulfanilamide therapy, while unexplained bleeding from the gastrointestinal tract has been seen by us on one or two occasions in cases in which sulfanilamide or sulfapyridine was being administered. One patient who was receiving sulfapyridine had such severe bleeding as to bring about death. Occasionally cases are encountered in which the administration of sulfanilamide produces severe attacks of diarrhea.

COMMENT

It is obvious from this description of the toxic manifestations of sulfanilamide and its derivatives that certain deductions can be made. We believe that, whenever possible, it is wise to utilize every available means of laboratory control in following patients who are receiving sulfanilamide or one of its derivatives. White blood cell counts, hemoglobin and urine examinations should always be done when circumstances permit this type of control. However, we are convinced that, with the exception of acute leukopenia, all the toxic manifestations of sulfanilamide or its derivatives which may occur in the first two weeks of therapy can be recognized by careful clinical observation, and we feel that no physician should hesitate to administer these drugs in therapeutically adequate amounts, provided he can see his patient at least once a day.

At the time the physician visits the patient who is receiving one of these drugs he should inquire as to his symptoms, especially in respect to headache, body aching or malaise, because these symptoms are often the precursors of many of the toxic reactions of sulfanilamide or its derivatives. In addition to an inquiry about symptoms, the scleras should be examined for the presence of jaundice, the mucous membranes for pallor and the skin for evidences of rash. The temperature should always be taken in order to detect whether drug fever is present, and if the patient says that he has been having chills and at the time that it is taken the temperature is normal, arrangements should be made to have the temperature taken frequently during the next twenty-four hours in order to determine whether or not fever is present.

No special precautions have to be observed in respect to the urine of patients who are receiving sulfanilamide, but it is highly important that the urine of patients who are receiving sulfapyridine or sulfathiazole be measured daily. This does not mean that the attendants or family of the patient have to record the urine volume in cubic centimeters or ounces, but any standard measure, whether it is only cups, will suffice. As a matter of fact, in the case of infants it would probably be satisfactory to record the number of voidings daily. In this way it is possible to detect an oliguria which may herald an approaching anuria. The daily examination of the urine under these circumstances should consist of a careful examination of a fresh specimen for gross blood, and at the same time instructions should be given to the patient's attendants to stop the drug and administer fluids in large quantities if the urine looks bloody.

Finally, one should always remember that if a patient has once had drug fever, rash, hepatitis, leukopenia,

acute hemolytic anemia, injection of the scleras and conjunctivas, diarrhea or purpura haemorrhagica in the course of therapy with sulfanilamide or its derivatives he is very likely to have a second, earlier and more severe toxic reaction if the drug is administered a second time. Therefore it is highly important to determine whether or not a patient has previously had a toxic reaction in the course of therapy with one or the other of these drugs. If he gives a history of a toxic reaction in the group which we have just enumerated, it is best to give a small test dose of the drug (0.3 Gm.) and observe the patient carefully over a period of twelve hours before cautiously beginning the course of therapy. Patients who have had a toxic reaction caused by one of these drugs may have a similar reaction when another member of the sulfonamide group is prescribed.

Special Articles

REPORT OF THE COMMITTEE ON
VISUAL ECONOMICS

The members of the Committee on Visual Economics during the past year have extended their effort toward bringing about a greater uniformity in the administration of compensation laws. A complete review of the compensation statutes and laws of all the states has been made (tables 1 and 2).

Table 1 sets forth the basic factors used by the different states in computing visual disability.

Read before the Section on Ophthalmology at the Ninety-First Annual Session of the American Medical Association, June 13, 1940.

TABLE 1.—Basic Factors Used in the Various States for Computing Visual Disability

States	Weeks Compensation for Loss of Use of One Eye	Weeks Compensation for Loss of an Eyeball	Percentage of Average Earnings, the Basis for Compensation	Visual Factors Used in Computations *	Visual Acuity Determined With or Without Correcting Lenses	Statutory Schedule Used	Snellen Notations Which Equal Industrial Blindness	Methods Used for Rating Permanent Partial Disability
Alabama.....	100	100	50	No adopted method or schedule
Arizona.....	108	130	50, 55 and 65	No adopted method or schedule
Arkansas.....	Compensation statute passed recently
California.....	No fixed number of weeks		61.75	1, 3, 4	With	Schedule F	Light perception	Special method
Colorado.....	104	139	50	1, 3, 4	Without	Schedule C	20/190	See table 2, schedule C
Connecticut.....	208	208	50	1	With	20/200	No adopted method or schedule
Delaware.....	113	113	50	No adopted method or schedule
Florida.....	100	100	50, 55 and 60	1, 2, 3, 4	With	Schedule D	20/170	A. M. A. method used
Georgia.....	100*	100	50	?	Without	?	?	No adopted method or schedule
Idaho.....	120	140	55	1	Without	Schedule D	20/200	See table 2, schedule D
Illinois.....	120	120	50	1	Without	Schedule B	20/200	See table 2, schedule B
Indiana.....	150	150	55	?	With	?	20/200	No adopted method or schedule
Iowa.....	100	100	60	No adopted method or schedule
Kansas.....	110	110	60	1, 2	Without	Schedule A	20/600	A. M. A. method used
Kentucky.....	100	100	65	1	Without	Schedule D	20/200	See table 2, schedule D
Louisiana.....	100	100	65	No adopted method or schedule
Maine.....	100	100	66%	1	With	Schedule A	20/200	A. M. A. method used
Maryland.....	100	100	66%	?	Without	?	?	No adopted method or schedule
Massachusetts.....	\$500	\$500	66%	No adopted method or schedule
Michigan.....	100	100	66%	No award for partial loss
Minnesota.....	100	100	66%	1	Without	Schedule B	20/200	See table 2, schedule B
Mississippi.....	No compensation law; common law applies
Missouri.....	108	118	66%	1, 2, 3, 4	Without	Schedule E	20/480
Montana.....	100	120	50 to 66%	?
Nebraska.....	125	125	66%
Nevada.....	108	130	60	1	With	Schedule D	20/200	See table 2, schedule D
New Hampshire.....	No adopted method or schedule
New Jersey.....	100	100	66%	20/200	No adopted method or schedule
New Mexico.....	100	100	55	?	No adopted method or schedule
New York.....	160	160 wks. and \$500	66%	1	With	20/100	Snellen notations regarded as fractional vision
North Carolina.....	100	100	60	1, 2, 3, 4	Without	Schedule A	20/200	A. M. A. method used
North Dakota.....	100	100	66%	1	With and without	Schedule A	20/800	A. M. A. method used
Ohio.....	125	125	66%	1, 2, 3, 4	With	Schedule A	20/800	A. M. A. method used
Oklahoma.....	100	100	66%	1, 2, 3, 4	With	Schedule A	20/800	A. M. A. method used
Oregon.....	\$1,000	\$1,000	None	1, 2, 3, 4	With and without	Schedule A	20/800	A. M. A. method used
Pennsylvania.....	125	125	65	Uses U. S. Bull. 406, Dept. of Labor
Rhode Island.....	80	80	50	?	With	20/200	No adopted method or schedule
South Carolina.....	100	100	50	No adopted method or schedule
South Dakota.....	100	100	55	No adopted method or schedule
Tennessee.....	100	100	50	1	With	Schedule B	20/200	See table 2, schedule B
Texas.....	100	100	60	?	With	?	Light perception	No adopted method or schedule
U. S. Gov't.....	160	160	66%	1, 2, 3, 4	With and without	Schedule A	20/200	A. M. A. method used
Utah.....	100	120	60	1	Without	Schedule G	20/230	See table 2, schedule G
Vermont.....	100	100	50	1	With and without	Light perception	No adopted method or schedule
Virginia.....	100	100	55	1	Without	Schedule B	20/200	See table 2, schedule B
Washington.....	\$1,080	\$1,440	None	1	Without	Schedule A	20/200	A. M. A. method used
West Virginia.....	132	132	66%	1	With	Schedule A	20/400	A. M. A. method used
Wisconsin.....	250	275	70	1, 2, 3, 4	With and without	Schedule A	20/800	A. M. A. method used
Wyoming.....	\$1,800	\$1,800	None	No adopted method or schedule

* 1 indicates central visual acuity at 20 feet; 2, central visual acuity at 14 inches; 3, visual fields; 4, muscle function (extra-ocular).

Table 2 sets forth schedules for loss of visual acuity which have been adopted by the designated states. Similar tables were compiled by Dr. Walter Small several years past. These have been revised and brought up to date and are herewith presented by the Committee on Visual Economics.

It may be noted that twenty-one states have adopted statutory schedules for loss of visual acuity, that one

In the report we find some omissions, some lack of clarity and some recommendations which have not met with general approval. Therefore the committee recommends:

1. That the committee be continued and that its membership be increased to three.

2. That the committee be requested to revise the report of 1925 and that a revised report be prepared,

TABLE 2.—Percentage Schedules Loss for Various Acuity Notations in Use Among the Different States

	Kansas Maine N. Carolina N. Dakota Ohio Oklahoma Oregon U. S. Gov't Washington Wisconsin W. Virginia	Illinois Minnesota Tennessee Virginia	Colorado	Idaho Kentucky Nevada Florida	Missouri	California	Utah
Visual Acuity	Schedule A	Schedule B	Schedule C	Schedule D	Schedule E	Schedule F	Schedule G
20/ 20.....	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
20/ 25.....	4.3%	5.0%	12.5%
20/ 30.....	8.5%	10.0%	10.0%	3.3%	12.0%	25.0%	5.0%
20/ 33.....	13.3%
20/ 35.....	12.5%
20/ 40.....	16.4%	20.0%	20.0%	11.0%	22.6%	37.5%	10.0%
20/ 45.....	20.0%
20/ 50.....	23.5%	25.0%	30.0%	16.5%	31.9%	50.0%	15.0%
20/ 60.....	30.1%	33.3%	40.0%	22.0%	40.0%	20.0%
20/ 70.....	36.0%	40.0%	45.0%	27.5%	47.3%	62.5%	25.0%
20/ 80.....	41.3%	50.0%	50.0%	33.0%	53.6%	30.0%
20/ 90.....	46.0%	62.5%	55.0%	38.5%	35.0%
20/100.....	51.1%	75.0%	60.0%	44.0%	64.1%	75.0%	40.0%
20/110.....	80.0%	65.0%	50.0%	45.0%
20/120.....	59.1%	65.0%	65.0%	50.0%	72.2%	50.0%
20/130.....	67.0%	75.0%	63.5%	55.0%
20/140.....	65.8%	69.0%	75.0%	65.0%	78.5%	60.0%
20/160.....	91.0%	80.0%	71.5%	65.0%
20/180.....	71.4%	93.0%	80.0%	77.0%	83.3%	70.0%
20/170.....	95.0%	85.0%	81.5%	75.0%
20/180.....	76.1%	97.0%	85.0%	85.0%	80.0%
20/190.....	99.0%	90.0%	88.0%	85.0%
20/200.....	80.0%	100.0%	90.0%	90.0%	90.0%	87.0%	90.0%
20/210.....	95.0%
20/220.....	83.3%	95.0%
20/280.....	100.0%
20/240.....	84.0%	94.0%
20/260.....	88.3%
20/267.....	93.0%
20/280.....	90.3%
20/300.....	91.8%
20/320.....	93.2%	97.9%
20/310.....	94.3%
20/370.....	95.2%
20/380.....	96.0%
20/400.....	96.7%	96.0%
20/450.....	97.9%
20/480.....	99.7%
20/500.....	98.6%
20/600.....	99.4%
20/700.....	99.7%
20/800.....	99.9%	99.0%

state has no compensation law, that one has passed a law which has not been adopted by the electorate, that twenty-five states have no legal schedule and that four states generally use the American Medical Association method but that in these states this has not been legally adopted.

The report of the Committee on Compensation for Eye Injuries was approved by this section and the House of Delegates fourteen years ago and the main principles contained therein are valid: the method for computing visual disabilities evolved therefrom has now become the legal statutory one in eleven states; in many other states in which no method has received legal sanction this method is employed by labor commissions and by ophthalmologists.

published and sent to all members of this section one month before the next annual meeting and that the revision be made a matter of special consideration at the meeting in 1941.

Respectfully submitted.

ALBERT C. SNELL, Chairman.
HARRY S. GRADLE.

Distribution of Iron in the Body.—Iron exists in the body of an adult in the hemoglobin of the red corpuscles and in all the cells of other tissues. The amount contained in the blood is about 3 Gm. That contained in invisible form in other cells has been estimated roughly at 1 to 3 Gm.—MacCallum, W. G.: A Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1940.

THE PHARMACOPEIA AND THE
PHYSICIAN

THE THERAPY OF RICKETS

EDWARDS A. PARK, M.D.

BALTIMORE

This is one of the second series of articles written by eminent authorities for the purpose of extending information concerning the official medicines. The twenty-four articles in this series have been planned and developed through the cooperation of the U. S. Pharmacopeial Committee of Revision and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.—ED.

Rickets can be prevented and cured in two ways: by irradiation of the skin with ultraviolet rays and by ingestion of vitamin D. How does it happen that the disease yields to two methods of treatment which seem so totally dissimilar? The answer is that, owing to a device of nature, the two lead to the same final result, namely the absorption of vitamin D into the blood. The skin is full of 7-dehydrocholesterol. Active ultraviolet rays, impinging on the skin, convert the 7-dehydrocholesterol, which is the provitamin form of D, into the vitamin form. The vitamin is then absorbed into the blood. If vitamin D is fed, it is absorbed from the small intestine. In the former case the vitamin was manufactured on the surface of the body as the result of chemical action of light; in the latter it entered the alimentary tract ready made.

NECESSARY INFORMATION CONCERNING VITAMIN D

It has now been shown that as many as eleven forms of vitamin D exist.¹ Of these, only two have a practical importance. The first is activated ergosterol, the second activated 7-dehydrocholesterol. Ergosterol is derived from plant sources. It is the form known as viosterol and the one in "metabolized" milk; i. e., milk activated as the result of feeding irradiated yeast to cows.² 7-dehydrocholesterol is the one formed in the skin under the action of ultraviolet light³ and probably also the one formed in milk through irradiation (irradiated milk).^{1a} Recent investigations have presented evidence of six different forms of vitamin D in cod liver oil.^{1c} It seems probable that the chief of these is 7-dehydrocholesterol. In the oils of other fish which have not as yet been studied by the newer methods applied to cod liver oil, evidence pointing to the existence of two biologically distinct forms of vitamin D has been brought forward,⁴ the one behaving like irradiated ergosterol, the other like activated 7-dehydrocholesterol. Naturally all forms of vitamin D are sterols, closely related chemically. For a discussion, the reader is referred to Bills.⁵ It is important to know that vitamin D is soluble in oil and most organic solvents but not in water. Bile acids appear to promote the absorption

of sterols (Schönheimer, Loeffler and Hummel, cited by Bills⁶). Heymann⁶ has reported that bile seems to be necessary for the absorption of vitamin D from the alimentary tract. It is also important to realize that vitamin D is not readily oxidizable and hence is more stable than vitamin A. The original discovery of vitamin D was made as the result of treating cod liver oil by means of oxygen and heat, which destroyed vitamin A but left vitamin D intact.⁷ It is far more stable than vitamins C and B₁.

No one knows how vitamin D acts. It has been proved by means of metabolism measurements that it increases the absorption of calcium and phosphorus from the alimentary tract. Evidence has been produced to show that it acts primarily in promoting the absorption of calcium.⁸ The absorption of phosphorus appears to be secondary. But undoubtedly vitamin D exerts action in the interior of the body also. It is known that it increases the metabolic rate.⁹ When Albright and Sulkowitch¹⁰ injected a phosphate solution intravenously into a patient suffering from intractable rickets, there was considerable increase in retention of phosphorus and a large increase in urinary excretion but the inorganic phosphorus levels in the blood serum remained unaffected. The important point is that the level of inorganic phosphorus in the blood remained the same, as if, in the presence of a vitamin D deficiency, the organism had lost the power to hold the inorganic phosphorus at the normal concentration. Albright and Sulkowitch believe that vitamin D acts directly on the kidney, stimulating the excretion of phosphate, and apparently that its regulatory influence on the blood is brought to pass through a regulation of absorption and excretion. It seems probable that vitamin D involves either directly or indirectly the parathyroid mechanism. The evidence, which is not very satisfactory, rests on the fact that the parathyroid glands are hypertrophied in rickets and infantile tetany (Erdheim;¹¹ Pappenheimer and Minor¹²). It seems reasonable to expect that it would involve parathyroid function, since the latter affects the calcium and phosphorus metabolism and the cellular mechanism concerned with the growth and destruction of bone.

WHAT IS A UNIT OF VITAMIN D?

The accepted standard unit for expressing the strength of vitamin D, as adopted by the League of Nations Health Organization and by the United States Pharmacopeia, is defined as "... the vitamin D activity

From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics of Johns Hopkins University School of Medicine.

1. (a) Bills, C. E.: New Forms and Sources of Vitamin D. *J. A. M. A.* 108: 13 (Jan. 12) 1937; (b) The Chemistry of Vitamin D, *ibid.* 110: 2150 (June 25) 1938. (c) Bills, C. E.; Massengale, O. N.; Hickman, K. C. D., and Gray, E. LeB.: A New Vitamin D in Cod Liver Oil, *J. Biol. Chem.* 126: 241 (Nov.) 1938.
2. Bethke, R. M.; Krauss, W. E.; Record, P. R., and Wilder, O. H. M.: The Comparative Antirachitic Efficiency of Vitamin D in Irradiated Milk, Metabolized (Yeast) Milk and Cod Liver Oil, *J. Nutrition* 11: 21 (Jan.) 1936.
3. Windaus, Adolf; Lettré, H., and Schenck, F.: Ueber das 7-Dehydrocholesterin, *Ann. d. Chem.* 520: 98, 1935.
4. Bills, C. E.; Massengale, O. N.; Imboden, Miriam, and Hall, Helen: The Multiple Nature of the Vitamin D of Fish Oils, *J. Nutrition* 13: 435 (April) 1937.
5. Bills, C. E.: Physiology of the Sterols, Including Vitamin D, *Physiol. Rev.* 15: 1 (Jan.) 1935.

6. Heymann, W.: Metabolism and Mode of Action of Vitamin D: IV. Importance of Bile in the Absorption and Excretion of Vitamin D, *J. Biol. Chem.* 122: 249 (Dec.) 1937.
7. McCollum, E. V.; Simmonds, Nina; Becker, J. E., and Shipley, P. G.: Studies on Experimental Rickets. XXI. An Experimental Demonstration of the Existence of a Vitamin Which Promotes Calcium Deposition, *J. Biol. Chem.* 53: 293 (Aug.) 1922.
8. Nicolaysen, R.: Studies upon Mode of Action of Vitamin D: Influence of Vitamin D on Fecal Output of Endogenous Calcium and Phosphorus in Rat, *Biochem. J.* 31: 107 (Jan.) 1937; Studies upon Mode of Action of Vitamin D: Influence of Vitamin D on Absorption of Calcium and Phosphorus in Rat, *ibid.* 31: 122 (Jan.) 1937.
9. Seel, H.: Ueber die Wirkung des weissen Phosphors und des Vitamin D (Vigantol) auf den respiratorischen Ruhezustand bei rachitischen jungen Ratten, *Arch. f. exper. Path. u. Pharmacol.* 140: 194, 1929. Baldwin, F. M.; Nelson, V. E., and McDonald, C. H.: Influence of Vitamin D Deficiency on Gaseous Exchange in Chicks, *Am. J. Physiol.* 85: 482 (July) 1928. Landelius, E., and Ljungkvist, G.: Experimental Research into Influence of Vitamin D on Oxygen Consumption of Growing Rats, *Skandinav. arch. f. Physiol.* 68: 252, 1934.
10. Nitschke, A., and Schneider, M.: Grundumsatzbestimmungen an rachitischen und rachitisch-tetanischen Säuglingen, *Ztschr. f. Kinderh.* 54: 1, 1933.
11. Albright, Fuller, and Sulkowitch, H. W.: The Effect of Vitamin D on Calcium and Phosphorus Metabolism: Studies on Four Patients, *J. Clin. Investigation* 17: 305 (May) 1938.
12. Erdheim, J.: Rachitis und Epithelkörperchen, *Denkschr. d. k. Akad. der Wissensch. Math-naturw. Klasse* 90: 363, 1914.
13. Pappenheimer, A. M., and Minor, J.: Hyperplasia of the Parathyroids in Human Rickets, *J. M. Research* 42: 391 (June-Sept.) 1921.

of 1 mgm. of the International Standard Solution of irradiated ergosterol found equal to 0.025 micrograms of crystalline vitamin D." This is the international unit (I. U.), accepted as the U. S. P. unit. The Steenbock unit is no longer used and need not be defined. In administering antirachitic agents one should think in terms of units of vitamin D, since that is the only way in which the dosages of the various substances containing vitamin D, which differ from one another so much in volume, can be reduced to a common denominator. For example, 1 teaspoon (4 cc.) of cod liver oil contains approximately 350 units, 1 quart (liter) of reinforced milk 400 units and 1 mg. of calciferol 400,000 units.

VITAMIN D IN FOODS

Vitamin D is contained in only a few foods ordinarily eaten by us, namely certain oily fishes and eggs. Herring, sardines, tuna and salmon, either fresh or canned, are fairly rich in the vitamin, as are also other fishes rarely eaten, such as the lamprey eel, the ray and the menhaden (Daniel and Munsell¹³). Eggs from all sources contain the vitamin. Fish roe is rich in it. Hen's eggs contain such variable amounts that they are not reliable sources. February eggs have been reported as yielding 140 units of vitamin D and June eggs 390 units per hundred grams.¹⁴ Drake¹⁵ states that it requires at least five egg yolks to furnish the vitamin D equivalent of 1 teaspoon of cod liver oil.

The foods that comprise the diet of the average person are almost lacking in vitamin D, since muscle meat, including the fat, kidneys and other glandular organs, fruit, sugar, cereal and vegetables (the leafy ones as well as seeds, bulbs and tubers) contain none or at the most traces. The amount in milk is negligible. Average butter is estimated as containing only 80 units per hundred grams, making its potency about one one-hundredth that of the average cod liver oil. Liver may contain a very small amount but not enough to have any practical value.

One can summarize this by saying that, although the diet may occasionally furnish appreciable amounts of vitamin D, most of the time it furnishes virtually none. The only proper attitude is to regard the diet as being completely devoid of the vitamin.

THE AVAILABLE SOURCES OF VITAMIN D

Cod Liver Oil.—According to the United States Pharmacopeia XI cod liver oil must contain at least 85 units per gram. However, probably all cod liver oil marketed in this country contains at least 100 units per gram. Some of the superior brands may contain two or even four times the official minimum standard. One teaspoon of cod liver oil, 4 Gm., supplies at least, therefore, 400 units. As already mentioned, the vitamin D in cod liver oil is probably chiefly activated 7-dehydro-cholesterol.

Cod liver oil is effective in rickets, infantile tetany and also osteomalacia, as was pointed out clearly years ago.¹⁶ It is universally obtainable and safe and in addition contains vitamin A (about 600 units per gram). The great disadvantage of cod liver oil is its fishy taste. Another disadvantage is its lack of concentration. Since it is not practicable to give more than 4 teaspoons

(16 cc.) daily, the maximum dosage is limited to 1,400 units. Cod liver oil is amply sufficient to prevent and to cure rickets in almost all instances. The older child or adult will not take cod liver oil because of its unpleasant taste. Infants, however, do not seem to mind the taste, provided the oil is given early and regularly. When the infant refuses cod liver oil, the fault usually lies with the mother or others who by words or actions communicate their feelings. If begun early and given regularly, ordinarily no difficulty is experienced in administration until toward the end of the first year. If the use is allowed to lapse, however, difficulties almost always arise. It is a common experience to find that when the cod liver oil is stopped for the summer its resumption in the fall is impossible. If cod liver oil is aspirated, it may produce lipoid pneumonia.¹⁷ For this reason it is inadvisable to give it to premature infants or infants with a very low vitality.

Many parents object to cod liver oil on the ground that it gives rise to digestive disturbances, especially in summer. The oil rarely does this and can be administered in hot weather without difficulty. However, some infants cannot take it, and in very rare instances hypersensitiveness has been reported.¹⁸ If infants do not readily take cod liver oil, it is wiser to turn elsewhere.

Cod liver oil is best administered from the spoon. It may, however, be floated on orange juice and the two fed with a spoon. It is possible in this way to give as much as 4 teaspoons in a single dose.

Viosterol in Oil.—Viosterol in oil is ergosterol activated by ultraviolet irradiation, dissolved in corn oil or some other bland oil. The United States Pharmacopeia XI requires that 1 Gm. of viosterol in oil shall contain "at least 10,000 units of vitamin D." One drop of viosterol as delivered by the special dropper included in the commercial viosterol package contains 222 units. Since there are variations in the quantity of oil delivered from droppers, the manufacturer supplies droppers which will deliver slightly more than the certified amount. For this reason actual dosage may slightly exceed calculation. Viosterol in oil is a hundred times stronger than standard cod liver oil in vitamin D content. At times its concentration is a great practical advantage.

Viosterol in oil has no taste; consequently no difficulty is encountered in its administration. In the case of the infant, it is best dropped directly into the mouth. It can, however, be dropped on orange juice in a teaspoon and in that way be floated into the mouth. The habit of adding viosterol to the feeding is bad, because a part of it may adhere to the sides of the bottle and be lost. The only disadvantage that viosterol has as compared with cod liver and other fish oils is that it does not supply vitamin A. Viosterol, on account of its tastelessness and concentration, is admirably suited for use by adults and older children.

Viosterol is now manufactured in at least two different ways, one by means of irradiation with short ultraviolet rays (the Steenbock patent), the other by means of bombardment with low velocity electrons (Knudson and Moore;¹⁹ Knudson;¹⁹ McQuarrie, Thompson,

13. Daniel, E. P., and Munsell, H. E.: Vitamin Content of Foods, Miscellaneous Publication 275, United States Department of Agriculture, 1937.

14. DeVaney, G. M.; Munsell, H. E., and Titus, H. E.: Effect of Sources of Vitamin D on Storage of the Antirachitic Factor in the Egg, Poultry Sci. 12: 215, 1933.

15. Drake, T. G. H.: Personal communication to the author.

16. Trouseau, Armand: Lectures on Clinical Medicine, Philadelphia, Lindsay & Blakiston, 1882, vol. 2, p. 734.

17. Goodwin, T. C.: Lipoid Cell Pneumonia, Am. J. Dis. Child. 48: 309 (Aug.) 1934.

18. Menagh, F. R.: Etiology and Results of Treatment in Angio-Neurotic Edema and Urticaria, J. A. M. A. 90: 668 (March 3) 1928.

19. Knudson, A., and Moore, C. N.: Comparison of the Antirachitic Potency of Ergosterol Irradiated by Ultraviolet Light and by Exposure to Cathode Rays, J. Biol. Chem. 81: 49 (Jan.) 1929. Knudson, A.: Further Studies on Antirachitic Activation of Substances by Cathode Rays, Science 66: 176 (Aug. 19) 1927.

Stoesser and Rigler²⁰). Viosterol made by either process seems to be the same chemically and biologically.

Viosterol (Calciferol) in Propylene Glycol.—Calciferol is activated crystalline ergosterol; in other words, the pure substance. This preparation is really just another form of viosterol. Its special merit lies in the solvent employed. Propylene glycol is soluble in water; hence viosterol in propylene glycol can be mixed directly with the milk. The only disadvantage is the one inherent in viosterol, namely the lack of vitamin A. It is standardized so that its potency corresponds exactly with that of viosterol in oil.

Fish Oils Enriched with Viosterol or Some Other Natural Source of Vitamin D.—Halibut liver oil is far richer than cod liver oil in vitamin A but only four times more potent in vitamin D. If viosterol or some fish oil highly concentrated in vitamin D is added to the halibut oil, it is possible to raise the vitamin D concentration to that of viosterol in oil and in that way obtain a product which is rich in both vitamins D and A. It is important to remember that practically the entire vitamin D content of the product is viosterol, if viosterol is used as the reinforcing agent. The vitamin A content of halibut liver oil is standardized at about 50,000 units per gram. The vitamin D content is exactly the same as that of viosterol. Administration is as described under viosterol in oil.

Fish Oils Naturally Concentrated in Vitamin D.—The oils from different species of fish vary greatly in concentration of vitamins A and D. Some are rich in A, some in D, many in both. The order of fish richest in vitamin D is the Percomorphi.²¹ In the preparation of the oil for therapeutic use the manufacturer has combined oils from various species in such a way that the final admixture has a concentration in vitamin D equal to that of viosterol in oil, namely 10,000 units per gram, and a concentration of vitamin A one hundred times that found in cod liver oil, namely 60,000 units per gram. These fish oils have the merit of providing vitamins D and A in high concentration so that both can be administered in doses measured in drops. The taste is fishy but the quantity required is small. Administration is as described under viosterol in oil.

Irradiated Cholesterol.—This is obtained by the ultraviolet irradiation of cholesterol exactly as viosterol is obtained through the irradiation of ergosterol. Its efficiency has been shown to be excellent by several different investigators (Hood and Ravitch;²² Drake, Tisdall and Brown²³) and has now been made available under the trade name "Delstarol."

Miscellaneous Preparations of Vitamin D Derived from Either the Fish Oils or Viosterol.—Viosterol is furnished in combination with dicalcium phosphate and the like. Concentrates from the fish oils are combined with carotene. Cod liver oil itself is concentrated and marketed in liquid, capsule or tablet form. The doses are indicated on the labels.

Vitamin D Milk.—Vitamin D can be placed in the milk in three different ways: first by ultraviolet irradiation,

second by feeding the cow irradiated yeast and third by adding a concentrate of vitamin D directly. The advantage of incorporating vitamin D in the milk is that it is taken automatically. The disadvantage is that the amount of the vitamin is determined by the milk requirement. In other words, the vitamin D may be insufficient though the milk sufficient. The requirement for vitamin D seems to be dependent on age rather than on weight.

(a) *Irradiated Vitamin D Milk:* Activation is accomplished through exposure to active ultraviolet rays from artificial sources. The irradiation is carried out in such a way that standardization is at 135 international units per quart. Attempts to obtain a higher potency have failed because of the production of an unpleasant taste. As already stated, the form of the vitamin in irradiated milk is probably activated 7-dehydrocholesterol. Irradiated milk is marketed fresh and also in evaporated and dried forms. The latter are standardized so as to have a potency of 135 international units to the reconstituted quart.

(b) *Metabolized Vitamin D (Yeast) Milk:* This is produced by feeding irradiated yeast to the cow. The standardization is 430 units per quart. The form of vitamin D is viosterol, as already stated.

(c) *Fortified Vitamin D Milk:* Vitamin D in the form of a concentrate derived from cod liver oil or the oils of other fishes or viosterol is added directly to the milk. Fortified vitamin D milk is standardized at 400 units per quart. The form of vitamin D in the milk varies naturally with the supplement.

Vitamin D Bread.—This contains 460 units in the form of viosterol per 24 ounce loaf. Six slices a day, or one-fourth loaf, would yield 115 units.

DO THE TWO MAIN FORMS OF VITAMIN D, 7-DEHYDROCHOLESTEROL AND VIOSTEROL, HAVE THE SAME BIOLOGIC VALUES FOR THE HUMAN BEING? DOES THE VEHICLE IN WHICH THE VITAMIN IS DISPERSED INFLUENCE UTILIZATION?

The discovery that cod liver oil, rat unit for rat unit, was far more effective in curing leg weakness in chickens than was viosterol suggested that the two forms of vitamin D used ordinarily in the treatment of rickets might have quite different biologic values. Indeed, Hess, Lewis and Rivkin²⁴ announced that the activity of cod liver oil and viosterol were different in the case of the human being, one rat unit of cod liver oil accomplishing the work of four rat units of viosterol. Soon afterward Hess, Lewis, MacLeod and Thomas²⁵ reported that metabolized milk, rat unit for rat unit, was more effective in the cure of rickets in the human being than either cod liver oil or viosterol, the efficiency equivalents being in the neighborhood of 1:1.25:5.2 respectively. In 1933 Hess and Lewis²⁶ published work which indicated that irradiated milk was even more potent than yeast milk when comparisons were made with viosterol.

More than forty studies²⁷ have been made in order to determine whether the two forms of vitamin D are

20. McQuarrie, Irvine; Thompson, W. H.; Stoesser, A. V., and Rigler, L. G.: The Antirachitic Potency of Ergosterol Activated by Low Velocity Electrons: Clinical Evaluation, *J. Pediat.* 10: 295 (March) 1937.

21. An order or suborder of teleosts, including all or most fishes with spines in their fins, such as the mackerel and bass.

22. Hood, J. S., and Ravitch, Irene: The Antirachitic Efficiency of Irradiated Cholesterol, *J. Pediat.* 11: 821 (Oct.) 1937.

23. Drake, T. G. H., Tisdall, F. F., and Brown, A. G.: A Comparison of the Antirachitic Effect of Irradiated Cholesterol and Cod Liver Oil, *J. Pediat.* 9: 421 (Oct.) 1936.

24. Hess, A. F.; Lewis, J. M., and Rivkin, Helen: Newer Aspects of the Therapeutics of Viosterol (Irradiated Ergosterol), *J. A. M. A.* 94: 1885 (June 14) 1930.

25. Hess, A. F.; Lewis, J. M.; MacLeod, F. L., and Thomas, B. H.: Antirachitic Potency of the Milk of Cows Fed Irradiated Yeast or Ergosterol: Clinical Test, *J. A. M. A.* 97: 370 (Aug. 8) 1931.

26. Hess, A. F., and Lewis, J. M.: An Appraisal of Antirachitics in Terms of Rat and Clinical Units, *J. A. M. A.* 101: 181 (July 15) 1933.

27. For the bibliography see Park, E. A.: The Use of Vitamin D Therapy, Preparations in the Prevention and Treatment of Diseases, *J. A. M. A.* 111: 1179 (Sept. 24) 1938.

equally effective in the case of the human being and whether vitamin D dispersed in milk is superior to vitamin D dispersed in oil. It was necessary to carry out these studies on infants. The task of obtaining an adequate number of reliable comparisons has been exceedingly difficult and a great deal of the work done has been of poor quality. Only generalizations of an uncertain nature can be drawn from the conflicting and confusing data obtained. For practical purposes the vitamin D in viosterol may be regarded as being equal to the vitamin D of cod liver oil. If viosterol is inferior to cod liver oil, rat unit for rat unit, the differences cannot be great. Vitamin D dispersed in milk is more effective than when dispersed in the usual oil menstrums. The three forms of vitamin D milk may be regarded for practical purposes as having equal value, rat unit for rat unit. However, evidence indicates that irradiated milk may be superior. Vitamin D milk having a potency of 400 units per quart will supply enough vitamin D to prevent the majority of full term infants from showing rickets. Evidence suggests, however, that irradiated milk has too low a potency (135 units per quart) to be relied on for this purpose. Four hundred units of vitamin D per quart of milk may be regarded as the minimum concentration in that menstrum for protection of the infant. The subject of the minimum dosage of vitamin D in the oil menstrums, *c. g.* viosterol in oil and cod liver oil, is so confusing that attempts at generalization are impossible. It is suggested in the case of the fish oils and viosterol that from 800 to 1,000 units daily be regarded as the lowest level that it is wise to employ for protection from rickets.

The rule that the physician should observe in prescribing vitamin D is to give enough to cover any possible requirement. There seems to be no reason to believe that amounts of vitamin D several times the minimum dosage have any deleterious effect.

HOW TO USE VITAMIN D FOR THE PREVENTION OF RICKETS AND INFANTILE TETANY

Since the period of greatest susceptibility to rickets is the first months of life, it is important that full dosage of vitamin D be reached early, certainly by the end of the second month. If cod liver oil is selected, it should be started at the beginning of the third week or at the latest the fourth week with a dose of one-half teaspoon (175 units). This dose can be increased to 1 teaspoon (350 units) after a few days. In the course of the next two weeks it should be raised to 2 teaspoons (700 units). This dosage may be enlarged to 1,000 units (3 teaspoons) or allowed to stand, according to need in the particular case. It is certainly advisable to give 3 teaspoons if for any reason the infant seems to be particularly liable to rickets. The dosage of 700 or 1,000 units should be continued throughout the first year. As much as 700 units should be continued throughout the second year.

If real difficulties in the administration of cod liver oil arise, it is advisable to turn to one of the other preparations of vitamin D. Difficulties often develop during the second year and are almost certain to develop if the administration of the oil is allowed to lapse for a time.

A real danger in the use of cod liver oil is that it may cause lipid pneumonia if it happens to run down the larynx into the lungs or is aspirated after vomiting. It should not be used if vomiting occurs frequently or if the infant is feeble or unable to swallow well. For the premature infant it is not sufficiently concen-

trated, and its use is somewhat risky from the standpoint of possible aspiration.

The use of the concentrated fish oils, viosterol in oil, the oils enriched with viosterol or irradiated cholesterol is exactly that advised in the case of cod liver oil itself. The administration should begin in the third or the fourth week, reach a dosage of 350 units in a week's time and by the end of the fifth or sixth week be increased to a dosage of 700 units. Depending on circumstances, this dosage of the vitamin D preparation should be allowed to stand or be increased to 1,000 units daily. This should be continued through the first year. A dosage of at least 700 units should be given during the second year.

The question is often asked if it is advisable to give cod liver oil or other antirachitic preparations during the summer, since in that season exposure to the sun's rays should of itself be sufficient to prevent the development of rickets. If one can be certain that exposure to the summer sun will be adequate, the administration of vitamin D is not necessary. From the practical point of view, however, it is a good plan to continue the vitamin through the summer, provided it is well taken, for the reason that resumption may be difficult or actually impossible.

If some form of activated milk is used as the antirachitic agent, as already indicated, the dosage is fixed not by the requirement of the child but by the amount of milk taken. This may or may not be sufficient to prevent rickets. Even though metabolized and fortified milks are potent enough in vitamin D to prevent rickets from manifesting itself in most children, it is safer to supplement them with at least 350 units of one of the preparations of vitamin D in oil during the first six months of life. If irradiated milk is given, it should be supplemented with vitamin D from some other source throughout the first year. Either metabolized or fortified vitamin D milk will probably supply sufficient vitamin D during the second year. Irradiated milk may be an adequate source of supply, but if doubt exists supplementation is advisable.

The premature infant is especially susceptible to rickets as well as to tetany, and occasional full term infants, especially Negro infants, seem particularly liable to develop rickets. If special susceptibility to rickets exists, the activated milks will not be satisfactory. They may be used, but they should be supplemented with liberal amounts of vitamin D from other sources. It is suggested that treatment be carried on as if the milk did not contain any vitamin D at all. The dosage of vitamin D required may be 5,000, 10,000 units or even more daily. If doses of these magnitudes are employed, one of the highly concentrated fish oils or viosterol in oil must be chosen, because the necessary quantity of cod liver oil would be too large to be taken. Often the physician discovers unusual susceptibility to rickets only when the ordinary preventive treatment proves insufficient. The course to pursue then is to increase the vitamin D until the desired therapeutic effect is obtained. It is suggested that periods of at least three weeks be allowed to elapse between increases, since at least that length of time is necessary for the full effect to declare itself. There need be no fear, however, in increasing the dose 1,000, 2,000 or 5,000 units at a time. Indeed, the increases ought to be made boldly.

The treatment of refractory rickets and the criteria which indicate that the dosage is adequate or exceeded will be given later.

HOW TO USE VITAMIN D FOR THE
CURE OF RICKETS

Although the doses of vitamin D which are sufficient to prevent rickets in a given case can be relied on to cure the disease, the cure may take place too slowly. It is better, therefore, to use sufficiently large doses to end the disease abruptly. The vitamin D milks are not sufficiently powerful antirachitic agents when the cure of rickets is at stake. If cod liver oil is employed, the curative dose in the ordinary case of rickets is 1,000 units (3 teaspoons) daily. This dosage, in the form of cod liver oil, the highly concentrated fish oils or viosterol preparations, will bring advanced rickets under control within a period of from three to four weeks in the great majority of cases. If doses larger than 1,000 units are required, it is best to turn to the concentrated preparations of vitamin D. In the case of premature infants, it is sometimes necessary to give as much as from 10,000 to 20,000 units to bring the disease to a complete termination in a short time, and in the case of some older children in whom the rickets is found to be obstinate it may be necessary to raise the dose to 60,000 units daily or even in excess of that amount. In any case, when the rickets has been stopped, as can be determined by means of repeated x-ray films or by measurements of calcium and inorganic phosphorus in the blood serum or, as can often be surmised from clinical examination alone, the dose of vitamin D can be reduced to protection levels. However, in the case of some infants and older children in whom the tendency to rickets seems to be especially highly developed, large doses of vitamin D may be required indefinitely. In the case of premature infants the need for large doses is usually temporary.

HOW TO USE VITAMIN D FOR THE
CURE OF TETANY

Since the initial action of vitamin D in some cases is to cause a depression of the serum calcium at the same time that it causes an elevation in the level of the inorganic phosphorus, it is advisable during the first few days of treatment also to give calcium in some form. If calcium chloride is chosen, it is usual to administer from 3 to 4 Gm. as an initial dose. This is to be followed by 1 Gm. four times a day for two or three days and then 1 Gm. twice a day. The administration of calcium can be stopped at the end of a week or ten days. But the vitamin D treatment should, of course, be continued as already described.

PERTINENT FACTS WITH REGARD TO THE
RELATIONSHIP OF ULTRAVIOLET
LIGHT TO RICKETS

The rays of ultraviolet light which are active in the cure of rickets lie between 313 and 230 millimicrons (Huldschinsky;²⁸ Hess and Anderson;²⁹ Sonne and Rekling³⁰). When the antirachitic power of individual wavelengths was tested by means of the monochromatic illuminator, it was found that the radiation at 313 millimicrons exerted a slight antirachitic effect, the radiations at 302, 297, 280, 265 and 253 millimicrons

exerted a strong effect, those at 248 and 240 millimicrons a feeble effect and those at 237, 220 and 200 millimicrons no antirachitic power whatever. Naturally the radiations which are active in the cure of rickets are those which the provitamin of vitamin D in the skin is able to absorb. It has been found that the provitamin ergosterol, which happens to have been the one extensively studied although not the one present in the skin, absorbs strongly from 305 to 230 millimicrons but probably possesses some absorptive power beyond these limits in both directions.³¹

Sunlight.—Sunlight consists of visible rays varying in length from 380 to 760 millimicrons (39 per cent), invisible infra-red rays from 760 to 50,000 millimicrons (60 per cent), those longer than 4,000 millimicrons amounting to only 1 per cent and invisible ultraviolet rays from 380 to 290 millimicrons (1 per cent). The distribution of the energy in the solar spectrum is continuous. Of course, the radiations from the sun actually extend far into the ultraviolet spectrum. But the atmosphere that surrounds the earth filters out all radiations which are shorter than 290 millimicrons even under the most favorable atmospheric conditions of summer (Fabry and Buisson;³² Dorno³³). In winter the atmosphere does not permit the passage of rays shorter than 306 millimicrons (Dobson and Harrison;³⁴ Dobson, Harrison and Lawrence;³⁵ Buisson³⁶), as will be explained presently. It is thus seen that the rays of the sun which reach the surface of the earth are at best very poorly represented in the ultraviolet spectrum and in particular in that part of it which is active in rickets.

The interposition of the atmosphere and the movement of the earth around the sun combine to cause a seasonal variation in both the quantity and the quality of the antirachitic radiations which reach the earth's surface. The reason for this is that, if the altitude of the sun is high, the short antirachitic radiations strike the earth more nearly perpendicularly and hence encounter a minimal thickness of atmosphere and sustain a minimal loss through absorption. At the same time their density per unit area is maximal. On the other hand, if the altitude of the sun is low, so that the short radiations strike the earth obliquely, they traverse a greatly increased thickness of atmosphere and suffer a correspondingly great loss through absorption. At the same time their density per unit area is diminished. At best the energy of the short rays at the extreme end of the spectrum, whether in winter or in summer, is very small. The intensity of the summer radiation at 290 millimicrons is reduced from its passage through the atmosphere two million times and possesses only one millionth the strength of the radiation at 315 millimicrons. Measurements in Baltimore¹ revealed that the total energy of the solar radiations between 290 and 315 millimicrons is from twelve to fourteen

31. Cox, W. M., Jr., and Bills, C. E.: Antirachitic Substances: On Relation of Isoergosterols to Vitamin D, *J. Biol. Chem.* 88: 709 (Oct.) 1930.

32. Fabry, C., and Buisson, H.: A Study of the Ultraviolet End of the Solar Spectrum, *Astrophysical J.* 54: 297, 1921.

33. Dorno, C.: Die physikalischen Grundlagen der Sonnen- und Himmelsstrahlung und ihre Anwendung in der Therapie, *Strahlentherapie* 18: 721, 1924.

34. Dohson, G. M. B., and Harrison, D. N.: Measurements of the Amount of Ozone in the Earth's Atmosphere and Its Relation to Other Geophysical Conditions, *Proc. Roy. Soc. London*, s.A 110: 660, 1926.

35. Dohson, G. M. B.; Harrison, D. N., and Lawrence, J.: Measurements of the Amount of Ozone in the Earth's Atmosphere and Its Relation to Other Geophysical Conditions: Part III, *Proc. Roy. Soc. London*, s.A 122: 456, 1929.

36. Buisson, H.: Mesures de l'ozone de la haute atmosphère pendant l'année 1927, *Compt. rend. Acad. d. sc.* 186: 1229, 1928; Mesures de l'ozone de la haute atmosphère pendant l'année 1928, *ibid.* 188: 647, 1929.

28. Huldschinsky, K.: Heilung der Rachitis durch künstliche Höhen-sonne, *Deutsche med. Wchnschr.* 45: 712 (June 26) 1919; Die Behandlung der Rachitis durch Ultraviolettstrahlung, *Ztschr. f. orthop. Chir.* 39: 426, 1920.

29. Hess, A. F., and Anderson, W. T. Jr.: Antirachitic Activity of Monochromatic and Regional Ultraviolet Radiations, *J. A. M. A.* 89: 1222 (Oct. 8) 1927.

30. Sonne, Carl, and Rekling, Eigil: Behandlung experimenteller Rattenrachitis mit monochromatischem ultraviolettem Licht, *Strahlentherapie* 25: 552, 1927.

times greater in summer than in winter.³⁷ It is necessary to think, therefore, of the solar spectrum in the temperate zone as undergoing a periodic expansion and retraction at the ultraviolet end, the expansion reaching its maximum at the summer solstice and the retraction being greatest at the winter solstice. The higher the latitude, the longer is the famine period in antirachitic radiation. At the polar region this famine is complete for the greater part of the year. Conversely, the lower the latitude the shorter the famine period. In the equatorial zone there is no famine, since the lowest altitude of the sun is sufficient to insure throughout the year adequate antirachitic radiation. Clark found that in Baltimore the antirachitic ultraviolet light in sunlight was least in December, began rapidly to increase in February, reached its height in late July or early August and then declined rapidly to its lowest point in December. The quantity of antirachitic radiations in March and October corresponded. This subject has been approached experimentally by exposing rachitic rats to sunlight at different times of the year.³⁸ During December, January and February it was found that sunlight had a slight but definite antirachitic action; a sharp increase in activity occurred about February 15 which reached the maximum in midsummer, and an equally sharp decrease began about October 15. The antirachitic power of sunlight in midsummer was found to be eight times greater than in midwinter. In Toronto the crucial inclination of the sun, as measured in terms of the antirachitic radiation, was about 35 degrees. This seasonal variation in rickets was first described in 1884.³⁹

Diurnal variations in the antirachitic ultraviolet radiations also occur. During the early morning and late afternoon, when the altitude of the sun is low, sunlight does not possess any antirachitic activity. Naturally, the period of the day when sunlight is effective against rickets is longer during the summer than during the winter. At Toronto in June the sun exerted an antirachitic effect from 7:55 a. m. to 4:30 p. m., but on March 6 this marked antirachitic action was present only from 10:37 a. m. to 2:18 p. m.⁴⁰ In Baltimore it was found that in the winter there were no antirachitic radiations in direct sunshine after 3 p. m. (Clark).

The ultraviolet radiations of the sun may reach the body either directly or as the result of reflection. The reflected rays are known as sky shine, the direct rays as direct shine. On meeting the atmosphere the solar radiations active in rickets are in part reflected and scattered. The cause of the reflection is to be found in the minute drops of water floating in the atmosphere. An infant placed in the shade is bathed only in sky shine. If placed at the far end of a room in the shaft of sunlight shining through an open window it is bathed only by direct shine. If placed in the direct sunlight outdoors in some unobstructed place which permits reflected rays to come in from the sides, the

infant receives both direct and sky shine. To receive all the sky shine, no obstruction can exist between the recipient and the dome of the sky. From the practical point of view, an infant in the shade against a wall receives only 50 per cent of the sky shine. The walls of buildings in cities greatly reduce sky as well as direct shine.

It is important to have some notion of the relative values of sky shine and direct shine as sources of antirachitic rays. In Baltimore in midsummer at noon on clear days the sky shine in the antirachitic range possesses about two thirds the value of the corresponding direct shine; in early spring and fall it has about an equal value and in winter a greater value (Clark). The ultraviolet radiation in sky shine is far more constant than is that of the direct sunshine. Since the reflected ultraviolet rays come from the drops of water in the atmosphere, their intensity may be actually increased by light clouds or haze. Therefore, on a cloudy day the total ultraviolet intensity of sky shine may be far greater than that of direct shine. On the other hand, if the clouds are dense the ultraviolet rays from sky shine also may be greatly reduced. When the altitude of the sun is high the ultraviolet radiation of sky shine is greater and hence the value of sky shine is greatest in summer and at noon. But, because sky shine is reflected light, its ultraviolet rays are transmitted to the earth when the altitude of the sun is too low for the direct radiation to penetrate effectively. Hence in the early morning and late afternoon the ultraviolet in sky shine may be greatly in excess of direct shine. Sky shine does not always but undoubtedly can produce tanning.

Ultraviolet radiation, both direct and indirect, may be reflected from favorable surfaces; for example, water, sand and snow.

Altitude as well as latitude is important in relationship to the transmissibility of the antirachitic ultraviolet radiations. The higher the altitude, the thinner the covering of atmosphere that absorbs the short radiations. In Denver (altitude 5,300 feet, latitude 40 degrees), the theoretical rickets period begins on December 1 and ends on January 17, whereas in Toronto (altitude 300 feet, latitude 44 degrees) it begins on October 15 and ends on February 15.

Foreign particles in the air, such as dust and smoke, act as absorbents of ultraviolet light. The smoke and dust of cities have greatly reduced the amount of ultraviolet light which penetrates to the street. Clothing completely absorbs the ultraviolet radiation of the sun. Theoretically, rayon material may permit the passage of antirachitic radiation.

Both intensity and time factors are concerned with the therapeutic effect of ultraviolet light in rickets. For example, a long exposure to ultraviolet light when little exists may be the equivalent of a short one under more favorable conditions. Clark estimated that in Toronto exposure of approximately twenty minutes to the noon sun in June was equivalent to three or four hours in January.

As stands to reason, the exposure of the entire body or large parts is more effective than the exposure of a small part. It is important to realize, however, that the exposure of the arm alone in a case of rickets is sufficient to cause a general deposition of lime salts (Huldschinsky).

Pigmentation of the skin is nature's method of protecting the dermis. Irradiation if sufficiently intense

37. Clark, J. H.: Annual Variation in the Antirachitic Radiation from Sun and Sky in Baltimore, *Am. J. Hyg.* 12: 690 (Nov.) 1930; The Zinc Sulfide Method of Measuring Ultraviolet Radiation and the Results of Three Years' Observation on Baltimore Sunshine, *J. Optic. Soc. America* 21: 240, 1931.

38. Tisdall, F. F., and Brown, Alan: Seasonal Variation of Antirachitic Effect of Sunshine, *Am. J. Dis. Child.* 34: 721 (Nov.) 1927; *ibid.* 36: 734 (Oct.) 1928.

39. Kassowitz, Max: Die normale Ossifikation und die Erkrankungen der Knochensysteme bei Rachitis und hereditärer Syphilis. II. Theil: Rachitis, Vienna, Wilhelm Braumüller, 1882; Tetanie und Autointoxication im Kindesalter, Wien. med. Presse 38: 97, 1897; *ibid.* 38: 139, 1897.

40. Tisdall, F. F., and Brown, Alan: Relation of Altitude of Sun to Its Antirachitic Effect, *J. A. M. A.* 92: 860 (March 16) 1929.

and prolonged will cause ulceration of the deeper layers if all pigment is lacking. However, the horny layer of the epidermis is a defense against ultraviolet light, since it absorbs the ultraviolet rays. "The pigment layer is the sun-shade for the dermis as the horny layer is the sun-shade for the epidermis."⁴¹ Radiation is curative of rickets in the Negro in spite of the heavy pigmentation. This indicates the superficiality of the seat of action of ultraviolet light. Ultraviolet light can penetrate the living skin of the rabbit a distance of from 1 to 2 mm.⁴²

Window glass removes all radiations shorter than 315 millimicrons. Behind window glass, therefore, sunlight, no matter how rich in active rays, will not exert any antirachitic effect. A variety of substitutes for window glass have been developed, some of which transmit 50 per cent or more of the antirachitic radiations. In an ordinary room, as an object is moved farther and farther away from a window, the area of sky becomes so small that the quantity of reflected rays which can reach the object become virtually nil. Unless an infant, therefore, is placed, practically speaking, against the window itself, he cannot benefit from the reflected rays. The only rays to penetrate the interior of the room through the special glasses are the direct rays. Even if the exposure is the most favorable, the direct rays shine in only for a fraction of the day in a continually shifting shaft of light. Only if a room was constructed entirely of the special glass and placed where the view was open, e. g. on the top of a high building, so that the sky shine could enter from all sides, would the special glass have a considerable usefulness, but in winter it would have very little even so.

ARTIFICIAL SOURCES OF ULTRAVIOLET LIGHT

The artificial sources of ultraviolet light are the quartz mercury-vapor lamp and the carbon arc lamp, both far richer than the sun's rays. The quartz mercury-vapor lamp gives off an emission of infra-red (52 per cent) comparable to that in solar radiation, a much smaller percentage of visible light (33 per cent) and a wealth of ultraviolet light of wavelengths ranging from 310 to 250 millimicrons. Twenty-eight per cent of the total energy lies in the ultraviolet and 6 per cent in wavelengths shorter than 290 millimicrons, the extreme limit of the solar spectrum. The spectrum of the quartz mercury-vapor lamp is discontinuous, though this feature is not a detriment. Strong lines lie at 313, 302, 297 and 255 and weaker lines at 310, 270 and 265 millimicrons.

The carbon arc lamps vary in their emissions according as certain metals, e. g. strontium, nickel, cobalt, cerium, fluorine or iron, are incorporated in the carbon either singly or combined. The radiations are strong in the ultraviolet range between 320 and 230 millimicrons if iron is used; if strontium, in the infra-red. Metals may be combined in such a way as to furnish light of percentage composition not differing greatly from solar radiation.

THE USE OF SUNLIGHT FOR PROTECTION AGAINST RICKETS

In the temperate zone in the summer, sunlight can be relied on to protect against rickets, except in rare instances, provided the child is exposed outdoors. The infant cannot receive too much ultraviolet light from

the sun's rays, if the blond who "burns" is excepted. Infants, as they grow older, should be placed outdoors on every suitable occasion and should be allowed to profit by the sky shine, even when direct shine is not available. In the winter, sunlight cannot be relied on for protection from rickets. Indeed it is best to regard winter sunshine as almost devoid of antirachitic rays and hence to substitute other methods of protection. Sunlight in the summer is capable of curing rickets. But it is better not to rely on it for that purpose but to adopt other means which are measurable and certain in their results. These other means are the administration of vitamin D, as already recited, or exposure of the body to radiations from artificial sources of ultraviolet light.

Advice with regard to the best ways to expose infants to sunlight has been furnished in great detail by the United States Children's Bureau. Practical points are these: In spring, fall and summer, under favorable weather conditions, the baby can of course be exposed outdoors. In cold weather, however, it may be necessary to expose him indoors. In the latter event the baby must be placed in the direct rays of the sun (direct shine) with the window open. Care must be used to protect the eyes. This can be accomplished by varying the position, so that the direct rays do not shine into the eyes. A good plan in cold weather is to begin with exposure of the cheeks only and then extend to one extremity at a time. Large areas of the body can be exposed, a part at a time, without danger. Exposure of only a small part of the body for a short space of time is sufficient to produce a general antirachitic effect, if the sunlight happens to be rich in antirachitic rays. In warm weather large surfaces of the body can be exposed with impunity. It is important to remember that sky shine is as valuable as direct shine and at times more valuable and that it is available on cloudy days; also that in winter in the temperate zone only in the noon period are active rays available and at best they are of low intensity.

HOW TO EMPLOY THE ARTIFICIAL SOURCES OF ULTRAVIOLET LIGHT

Treatment with the quartz mercury-vapor lamp may be conducted as follows: The lamp is placed at a distance of 2 or 3 feet from the body, which of course is uncovered, and exposure of the front and back carried out alternately. The exposures are at first for one minute and are increased by one minute at each session until a total of ten minutes is reached. The treatment is carried out every day or every other day. It must be continued for at least a month. At the end of this time periods of exposure may be reduced to from two to three minutes every other day, or some other treatment may be substituted. For the prevention of rickets the irradiations may be carried out every other day and the duration of each session limited to two or three minutes. Treatment with the carbon arc lamp is conducted in a similar manner.

The quartz mercury-vapor lamp is more apt to cause burns than the carbon arc lamp. The burns produced by ultraviolet light are, however, exceedingly superficial (sunburn), and the inflammation disappears in a few days. When either lamp is used, the eyes must be protected. Irradiation with ultraviolet lamps is especially valuable in conditions in which vitamin D cannot be absorbed well from the intestine, e. g. obstruction of the bile duct. It also has been used to advantage in the protection and cure of premature babies. The

41. Miescher, G.: *Das Problem des Lichtschutzes und der Lichtgewohnung, Strahlentherapie* 35: 403, 1930.
42. Anderson, W. T., Jr., and Macht, D. I.: *Penetration of Ultraviolet Rays into Live Animal Tissue, Am. J. Physiol.* 86: 320 (Sept.) 1928.

quartz mercury-vapor lamp and the carbon arc lamp may be used to supplement administration of vitamin D. When the carbon arc lamps are used, a curative effect may be obtained even though no tanning is produced. The quartz mercury-vapor lamps cause tanning. Tanning is a useful sign that ultraviolet light is producing an antirachitic action. Obviously, the use of the quartz mercury-vapor lamp and of the carbon arc lamp is contraindicated in blonds who "burn" and do not tan. For such individuals it is better to rely on the administration of vitamin D.

THE TREATMENT OF REFRACTORY RICKETS

Refractory rickets is most commonly seen in children over 3 years of age (late rickets), probably because by then the refractory forms have been sifted out. The clinical manifestations, as well as the x-ray, serologic and metabolic, are essentially the same as those in the ordinary infantile form of the disease, although the deformities may be somewhat different. The diagnosis of refractory rickets is arrived at only by trial and failure of vitamin D therapy (or irradiation) in ordinary doses.

Before the conclusion is reached that in a given case the rickets is refractory, it is most important to be certain that the disease is not a peculiar variety of endogenous origin, unrelated to vitamin deficiency, such as that described by a series of investigators (de Toni;⁴³ Fanconi;⁴⁴ Debré, Marie, Cléret and Messimy;⁴⁵ Schier and Stern;⁴⁶ Ullrich;⁴⁷ Schlesinger⁴⁸). The characteristic features of this form of endogenous rickets are glycosuria with a low blood sugar (renal diabetes), acidosis due to the presence of an unidentified organic acid, retardation in physical development (dwarfism) and rickets of an osteoporotic type, which may be extreme and characterized by extremely low inorganic phosphorus values in the serum. Another obscure and at present not clearly described variety of rickets of endogenous origin is earmarked by a disturbance of cystine metabolism and retardation of growth (Lignac;⁴⁹ Beumer and Wepler⁵⁰). Finally, the clinician must be certain that the case is not one of renal hyperparathyroidism (renal rickets; renal osteitis fibrosa). Endogenous rickets, such as has been mentioned, and renal hyperparathyroidism are uninfluenced by vitamin D therapy. In fact, in renal hyperparathyroidism vitamin D therapy may be actually dangerous.

After it has been determined that the type of rickets does not fall in the categories just mentioned, vitamin D therapy may be begun. The therapeutic secret seems to lie in the administration of extremely large doses of vitamin D. In the case of a boy of 16 years, reported by Albright, Butler and Bloomberg,⁵¹ it was necessary

to increase the dosage of vitamin D to between 1,100,000 and 1,500,000 units daily in order to obtain definite evidence of healing. At the present time it is necessary to give the child 150,000 units daily in order to prevent a recurrence of the disease.⁵² In a similar case in a 7 year old child, presently to be reported by Guild and Wilkins, it has been necessary to raise the dosage to 300,000 units daily. In the case reported by Albright, Butler and Bloomberg the first positive indication that the enormous doses of vitamin D were effective was in the calcium-phosphorus metabolism. The calcium-phosphorus balance became positive and the loss of calcium in the stools greatly diminished. This change in excretion occurred without demonstrable change in the level of the inorganic phosphorus of the blood serum. Subsequently, however, the inorganic phosphorus of the blood serum rose slightly. In Guild's case the evidences were active deposition of lime salts at the ends of the growing bones. This was accompanied by a very slight increase in the level of the inorganic phosphorus in the serum. The important point is that in these refractory cases, as nearly as one can judge from two instances, the effect of the very large doses of vitamin D on the level of the inorganic phosphorus in the blood serum was very slight. In both the cases mentioned, the difficulty did not lie in the absorption of vitamin D. In Guild and Wilkins' case measurements of the vitamin D in the blood serum showed that it was present in 200 times the level regarded by Warkany⁵³ as being normal.

The cure of rickets experimentally produced in the rat by means of citric acid-sodium citrate solution has been described by Hamilton and Dewar⁵⁴ and Shohl⁵⁵ and recently a curative action in the case of two infants has been reported by Shohl and Butler.^{55a}

The mode of action of the citric acid-sodium citrate combination in rickets is not known. The hypothesis which led to the trial of the citric acid treatment was that an alkaline effect in the intestine and an acid effect in the body would favor the development of rickets, whereas an acid reaction in the alimentary tract and an alkaline effect in the body would oppose its development. The citric acid-sodium citrate solution theoretically would tend toward the production of an acid state in the alimentary tract and an alkaline one in the body. A tartaric acid and sodium bitartrate solution was discovered by Hamilton and Dewar to be effective. However, Shohl found that malic, malonic and succinic acids were not effective. A possible factor in the "citrate effect" may lie in a peculiarity of the compound which calcium forms with citric acid. "Shear and Kramer and Shear, Kramer and Resnikoff showed that a solution of sodium citrate, added to a solution containing calcium ions, removes the calcium ions from the solution and that the calcium ions are bound by the citrate ions in some kind of soluble slightly ionized complex, the exact nature of which is unknown" (Hamilton and Dewar). A further peculiarity lies in the fact that healing takes place under the influence of the citric acid-sodium citrate treatment at calcium and phosphorus levels in the blood below those considered essential for

52. Albright, Fuller: Personal communication to the author.

53. Warkany, J.: Estimation of Vitamin D in Blood Serum, *Am. J. Dis. Child.* 52: 831 (Oct.) 1936.

54. Hamilton, Bengt, and Dewar, Margaret M.: Effect of Citrate and Tartrate on Experimental Rickets, *Am. J. Dis. Child.* 54: 548 (Sept.) 1937.

55. Shohl, A. T.: Effect of Acid-Base Content of Diet upon Production and Cure of Rickets with Special Reference to Citrates, *J. Nutrition* 14: 69 (July) 1937.

55a. Shohl, A. T., and Butler, A. M.: *New England J. Med.* 220: 515 (March 23) 1939.

43. de Toni, G.: Remarks on the Relations Between Renal Rickets (Renal Dwarfism) and Renal Diabetes, *Acta paediat.* 16: 479, 1933.

44. Fanconi, G.: Der frühinfantile nephrotisch-glykosurische Zwergwuchs mit hypophosphatämischer Rachitis, *Jahrb. f. Kinderh.* 147: 299, 1936.

45. Debré, Robert; Marie, Julien; Cléret, F., and Messimy, R.: Rachitisme tardif coëxistant avec une néphrite chronique et une glycosurie, *Arch. de méd. d. enf.* 37: 597 (Oct.) 1934.

46. Schier, A., and Stern, A.: Ueber einen Fall von unheilbarer Rachitis, *Arch. f. Kinderh.* 78: 176 (June) 1926.

47. Ullrich, O.: Ueber neuere Behandlungsvorfahren der englischen Krankheit im Dienste der allgemeinen Rachitisbekämpfung: Versager der Rachistherapie und Tier-rachitis, *München. med. Wchnschr.* 76: 1433 (Aug. 23) 1929.

48. Schlesinger, Bernard: Renal Dwarfism and Rickets, *Proc. Roy. Soc. Med.* 25: 10 (Nov.) 1931.

49. Lignac, G. O. E.: Ueber Störung des Cystinstoffwechsels bei Kindern, *Deutsches Arch. f. Klin. Med.* 145: 139 (Oct.) 1924.

50. Beumer, H., and Wepler, W.: Ueber die Cystinkrankheit der ersten Lebenszeit, *Klin. Wchnschr.* 16: 8 (Jan. 2) 1937.

51. Albright, Fuller; Butler, A. M., and Bloomberg, Esther: Rickets Resistant to Vitamin D Therapy, *Am. J. Dis. Child.* 54: 529 (Sept.) 1937.

the deposition of lime salts in bone. For example, Shohl and Butler discovered lime salt deposition occurring in the bones of one of their rachitic children when the serum calcium concentration was 8.7 and the inorganic phosphorus concentration 3.1 mg. per hundred cubic centimeters. In their other case, healing was noted when the serum calcium was 6.3 and the inorganic phosphorus 3.8 mg. per hundred cubic centimeters. Under the influence of the therapy the serum calcium falls and the inorganic phosphorus rises slightly. The same phenomenon has been noted in the rat. Healing was observed as early as from six to nine days after the treatment was commenced and perhaps actually occurred earlier. With the low calcium value concentration tetany was not produced.

Shohl and Butler used 20 cc. molar citric acid and 30 cc. molar sodium citrate. This was added to the formula as a diluent. They are inclined to think, however, that citric acid in excess of the sodium citrate would have been preferable and suggest two parts molar acid to one part molar salt.

Chaney and Blunt^{55b} reported fifteen years ago that orange juice, from 600 to 700 cc. daily, increases the calcium, phosphorus retention and, to a lesser extent, the magnesium retention in the human being. Orange juice can cure rickets, as attested by personal experience. But the curative effect will disappear as soon as the orange juice therapy is stopped. The amount of the citrate used by Shohl and Butler in the treatment of their two infants suffering from rickets was equivalent to that furnished by "five to six large oranges."

We do not recommend the citric acid-sodium citrate treatment of rickets as a substitute for the vitamin D treatment but only as a method to be employed under special circumstances, perhaps in conjunction with vitamin D treatment. Albright and Sulkowitch^{55c} reported beneficial results from the administration of the citrate mixture in a patient with nephrocalcinosis. Unfortunately, the citric acid-sodium citrate treatment has been found to be useless in cases of rickets refractory to vitamin D treatment.^{55d}

Successful treatment by means of the administration of alkali in certain unusual cases not understood has been reported (Boyd;⁵⁶ Bornscheuer;⁵⁷ Stearns and Warweg⁵⁸).

Finally, attention is called to the fact that in obstructive jaundice vitamin D is not absorbed well from the alimentary tract. Under conditions in which the flow of bile into the intestine does not take place, it is advisable to treat rickets by means of ultraviolet light.

HOW TO INDUCE RAPID HEALING

In so-called thoracic rickets, described by Park and Howland,⁵⁹ the weakness of the thorax is a menace to the life of the child. In such cases it is advisable to supply rigidity with the least possible loss of time. In the case of a baby aged 8 months suffering from very

advanced rickets, one can give daily doses of 50,000 units of vitamin D. When the healing begins, as can be detected by means of x-ray films or calcium and inorganic phosphorus determinations, the dosage should be reduced to the ordinary curative levels. Several investigators (Harnapp;⁶⁰ Bischoff;⁶¹ Schirmer⁶²) have tried the use of enormous single doses of vitamin D, e. g. 600,000 units, and have reported that no bad effects result. It has been shown recently that after a single large dose of vitamin D the vitamin remains in the body for a number of weeks.⁶³ I do not recommend the single dose method. To the infant as much as 50,000 units of vitamin D can be given daily with safety for two or three weeks. If the dose is continued longer, one must watch for toxic effects.

HOW TO DETERMINE THAT VITAMIN D THERAPY IS SUCCEEDING

The best way to determine whether vitamin D is succeeding is by measurements of the calcium and inorganic phosphorus in the blood serum or x-ray examination or preferably both. If the level of the calcium is normal and the inorganic phosphorus rises to 5 mg. per hundred cubic centimeters or above, one knows that a curative effect has been obtained. In cases of ordinary rickets, treated with the usual doses of vitamin D, a rise in the inorganic phosphorus level of the blood serum can be expected on about the tenth day. If very large doses of vitamin D are given, the rise in the level of inorganic phosphorus of the blood serum may occur as early as the fifth or sixth day after the beginning of treatment. Under ordinary conditions the first evidence of deposition of lime salts at the ends of the long bones occurs about the twenty-first day. But if very large doses of the vitamin are given, signs of deposition may be found on the tenth day. When enormous doses of vitamin D have been given, doses in the hundred thousands of units, the signs of deposition in the x-ray films have been reported on the fifth or sixth day. If the physician is obliged to rely on inspection and palpation in order to gage the effect of antirachitic treatment, it is very difficult to be certain that the cure has begun. The recession of the deformities is a very gradual process. Perhaps the most obvious clinical indication that the treatment is successful, but one that is hard to appraise, is improvement in muscle function. The child begins to make efforts to walk or to sit up. He seems stronger or more active. Very gradually the deformities of the cartilage-shaft junctions vanish and the bones seem to have acquired an increased degree of rigidity.

If the x-ray appearance is used as a guide to the effectiveness of treatment, it is important to remember that the filling in process of the ends of the bones in extreme rickets requires from two to three months and that the pattern of the lesion will remain visible in the roentgenogram for months after the disease has been completely arrested.

SIGNS OF TOXICITY OF VITAMIN D

One need not fear that the dosage of vitamin D will be toxic unless renal insufficiency exists or unless the dosage is extremely large. To adults, enormous doses

55b. Chaney, M. S., and Blunt, K.: *J. Biol. Chem.* **66**: 829-846 (Dec.) 1925.

55c. Albright, Fuller; Consolazio, W. V.; Coombs, F. S.; Sulkowitch, H. W., and Talbott, J. H.: *Bull. Johns Hopkins Hosp.* **66**: 7-33 (Jan.) 1940.

55d. Shohl: Personal communication to the author.

56. Boyd, J. D.: *Endogenous Rickets*, *Proc. Soc. Exper. Biol. & Med.* **26**: 181 (Dec.) 1928.

57. Bornscheuer, P.: *Ein Fall von endogener gegen D-Vitamin und Licht resistenter perennierender Rachitis*, *Ztschr. f. Kinderh.* **51**: 56, 1931.

58. Stearns, Genevieve, and Warweg, Edna: *Studies of Phosphorus of Blood, Phosphorus Partition in Whole Blood and in Serum and Serum Calcium and Plasma Phosphatase During Healing of Late Rickets*, *Am. J. Dis. Child.* **49**: 79 (Jan.) 1935.

59. Park, F. A., and Howland, I.: *The Dangers to Life of Severe*

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61. Bischoff, H.: *Rachitisbehandlung mit konzentrierten Vigantol*, *Jahrb. f. Kinderh.* **150**: 2, 1937.

62. Schirmer, R.: *Rachitisbehandlung mit einmaliger Vitamingabe*, *Monatschr. f. Kinderh.* **68**: 269, 1937.

63. Heymann, Walter: *Metabolism and Mode of Action of Vitamin D: Different Tissues in Vivo*, *J. Biol. Chem.*

of vitamin D have been given over long periods without apparent injury. The symptoms of overdosage seem to be nausea, headache, diarrhea, loss of appetite, frequent micturition and nocturia and lassitude.⁶⁴ In the case of the ordinary full term baby more than 3 months of age I regard 50,000 units as lying in the danger zone if given for more than two weeks. For small premature babies I believe that signs of overdosage ought to be watched for if more than 20,000 units is given daily for more than two weeks. Reed⁶⁵ assures me that the toxic effects of vitamin D are independent of its action in raising the calcium and inorganic phosphorus concentration in the blood serum. However, in treating rickets with correction of the disturbance of the calcium and phosphorus metabolism as the main objective, the elevation of calcium above 12 mg. per hundred cubic centimeters is an indication that the dosage has been exceeded and ought to be reduced. With a rise in the serum calcium, a rise in inorganic phosphorus takes place. But this may not reach even the normal level. If the excessive vitamin D therapy is continued, undoubtedly the inorganic phosphorus, as well as the calcium, will become much elevated, and metastatic calcification will occur. In rickets great aid is furnished by the x-ray examination alone. If the x-ray film reveals shadows which indicate healing, the inference can be made that the vitamin has begun to act and that the desired effect of treatment has been gained.

Examination of the urine may reveal evidence of overdosage. Albright and his collaborators⁶¹ noted in their case of intractable rickets under treatment with enormous doses of vitamin D that the urine was loaded with calcium and contained many calcium casts such as have been observed in cases of hyperparathyroidism⁶⁶ and were able to infer from the presence of the calcium and the characteristic casts in the urine that the dosage of vitamin D had reached toxic proportions.

THE RELATIVE COST OF THE DIFFERENT PREPARATIONS OF VITAMIN D

Of the preparations of vitamin D in oil, cod liver oil is still the most economical. In terms of international units, some of the more expensive brands of cod liver oil are more economical than some of the cheaper brands. For example, oil selling at 50 cents a pint and having only the required 85 units per gram costs twice as much per 1,500 units as a very high grade of oil, sold at 90 cents a pint but containing 350 units per gram. The oils depending for their enrichment on viosterol cost in general twice as much as the concentrated fish oils. The fish oils highly concentrated in vitamin D are as economical sources as many of the poorer brands of cod liver oil. Irradiated milk is about one third as economical as metabolized or reinforced milk. In each case the enrichment process adds about 1 cent per quart, so that the vitamin D milks are con-

siderably more expensive in terms of units than is cod liver oil or the concentrated fish oils. No extra charge is made for vitamin D in canned evaporated milk. The amount of the vitamin in the milk, however, is very low, being only 135 units per reconstituted quart.

It is my inclination to prefer cod liver oil or the concentrated fish oils to the viosterol preparations for the reason that it seems better to prescribe a preparation of vitamin D which is also rich in vitamin A than one which contains vitamin D alone.

The quartz mercury vapor lamps and the carbon arc lamps are expensive sources of vitamin D in comparison with cod liver oil. The quartz mercury vapor lamp costs more initially but is said to be less expensive to operate. However, these lamps are not necessarily expensive sources if large groups of children can be treated simultaneously, as is possible in institutions. The carbon arc lamps are the ones best suited for the purpose just mentioned.

Johns Hopkins Hospital.

CONFERENCES ON THERAPY

TREATMENT OF BLOOD DISORDERS

- X. EFFECTS PRODUCED BY DRUGS

NOTE.—These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments and institutions. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors.

DR. HARRY GOLD: In the series of conferences on the blood diseases that we have had in recent weeks, references have been made from time to time to the actions of drugs on the blood, more particularly in relation to their use as therapeutic agents. Here is a list of the more important ones:

1. Iron.
2. Copper.
3. Arsenic.
4. Benzene.
5. Phenylhydrazine.
6. Certain more complex organic materials (used in the treatment of pernicious anemia).

The list of agents that are useful in the treatment of blood diseases is small. Today we will consider in greater detail the effects of chemical agents on the blood and hemopoietic organs in persons without blood diseases.

This subject is encountered in practice in three general situations:

First, it presents problems in differential diagnosis. Stimulation of the vagus nerve produces eosinophilia. The parasympathetic drugs produce eosinophilia. A dose of pilocarpine, muscarine or barium can nearly double the white cell count in the circulating blood owing presumably to constriction of the smooth muscle of the spleen. A dose of epinephrine can cause a fairly pronounced increase of the red cell count. These do not directly act on the blood, but they certainly change the normal blood picture and are sources of confusion. Epinephrine causes hemoconcentration by its action in constricting the hepatic veins, as a result of which plasma passes out of the circulation and the red cell count goes up. Prolonged surgical anesthesia

64. Rappaport, B. Z., and Reed, C. I.: Viosterol of High Potency in Seasonal Hay Fever and Related Conditions, *J. A. M. A.* **101**: 105 (July 8) 1933. Dreyer, Irving, and Reed, C. I.: The Treatment of Arthritis with Massive Doses of Vitamin D, *Arch. Phys. Therapy* **16**: 537 (Sept.) 1935. Wyatt, B. L., Hicks, R. A., and Thompson, H. E.: Massive Doses of Vitamin D in the Treatment of Proliferative Arthritis, *Ann. Int. Med.* **10**: 534 (Oct.) 1936. Livingston, S. K.: Vitamin D and Fever Therapy in Chronic Arthritis, *Arch. Phys. Therapy* **17**: 704 (Nov.) 1936. Vrtiak, E. G., and Lang, R. S.: Observations on the Treatment of Chronic Arthritis with Vitamin D, *J. A. M. A.* **106**: 1162 (April 4) 1936. Farley, R. T.: Management of Arthritis, *Illinois M. J.* **71**: 74 (Jan.) 1937. Krafka, Joseph, Jr.: Simple Treatment for Psoriasis, *J. Lab. & Clin. Med.* **21**: 1147 (Aug.) 1936. Cedar, E. T., and Zon, Leo: Treatment of Psoriasis with Massive Doses of Crystalline Vitamin D and Irradiated Ergosterol: A Preliminary Report, *Pub. Health Rep.* **52**: 1580 (Nov. 5) 1937.

65. Reed: Personal communication to the author.
66. Albright, Fuller, and Bloomberg, Esther: Hyperparathyroidism and Renal Disease, with a Note as to the Formation of Calcium Casts in This Disease, *Tr. Am. A. Genito-Urin. Surgeons* **27**: 195, 1934.

with ether causes fairly pronounced leukocytosis. These matters are not given consideration very often because they really are not of serious consequence, but as I have said they can be a source of confusion. Autonomic effects and disturbances in the central nervous system cause diversified changes in the blood picture.

Second, the problem of the actions of drugs on the blood is encountered in connection with industrial poisoning.

Third, blood changes are encountered as side actions or toxic actions in the course of the use of drugs for therapeutic purposes.

How to manage these disturbances of the blood when they are due to a known agent would seem on the surface to be perfectly simple. The first answer that comes to mind is this: Discontinue the drug. That is all right in industrial poisoning, but in cases in which toxic effects arise in the course of the therapeutic uses of such a compound as sulfanilamide that answer falls short. If one cannot safely discontinue the drug, the question arises: How far can one go without producing irreparable damage? Some of these points may be cleared up in the course of the discussion today.

Once the point of view is shifted from agents used in the treatment of blood diseases to agents which affect the blood and the hemopoietic organs, the numbers that need to be considered mount steeply from the five or six that I have mentioned to literally hundreds and perhaps thousands of chemical agents.

There is hardly a major class of chemical agents that does not contribute members that disturb the blood and blood forming organs:

1. Alkaloids.
2. Glucosides.
3. The aliphatic hydrocarbons and their derivatives.
4. Benzene and its derivatives.
5. Metals.
6. Other chemicals.

The more important sites of their actions in disturbing the blood picture are:

1. The smooth muscle of organs in which the blood is stored, especially the spleen, or the smooth muscle of the hepatic vessels.
2. The bone marrow.
3. The elements in the circulating blood itself.

What kind of disturbances in the blood elements do drugs produce? I have here a list of changes that are encountered as the result of known compounds:

- Erythropenia.
- Erythrocytosis (polycythemia).
- Hemolytic anemia.
- Color index (may be high or low).
- Reduction of blood platelets.
- Purpura haemorrhagica.
- Leukocytosis.
- Lymphocytosis.
- Eosinophilia.
- Leukopenia.
- Granulocytopenia.
- Agranulocytosis.
- Myeloid leukemia.
- Combinations of the foregoing conditions.

That list is not complete, but I think it gives some idea of how widely diversified the changes are which chemical agents can produce in the blood.

In the bone marrow are also encountered the most diversified types of changes by drugs, from complete aplasia of all the elements at one extreme to the hyper-

plasia characteristic of pernicious anemia at the other; and between these all sorts of more or less specific pictures have been described.

There are also changes in the coagulation of the blood, which may be increased or decreased. Chloroform can produce an almost complete disappearance of the coagulability of the blood. A dose of epinephrine can increase the coagulability of the blood from 200 to 300 per cent. The significance of such effects on the blood is in certain situations very considerable.

Also there are changes in the hemoglobin, more commonly the production of methemoglobin and sulfhemoglobin.

Pharmacologists can take little pride or satisfaction in the state of our knowledge of the blood disturbances caused by drugs. The attack on these problems has not been at all systematic. There is, as a result, almost no knowledge as to how many of the more important chemical agents produce their effects on the blood and hemopoietic system, with but few exceptions. In a story that is so fragmentary, there is always a temptation to try to make some order by filling in the clinical gaps with the results of animal experiments. There great danger lies because there are such wide species differences in the response of the blood to chemical agents. Of course, species differences in response to drugs are not confined to the blood.

Just a few illustrations: A large dose of potassium chlorate produces methemoglobinemia readily in man, the dog and the cat, but the rabbit seems immune. Benzene poisoning in the animal is characterized predominantly by leukotoxic action; the destruction of red cells is more or less at a minimum. In man, on the other hand, chronic benzene poisoning is very often associated with severe grades of anemia. We have to be very cautious, in view of these facts, when we try to complete the story of mechanisms that operate in man, from the results of animal experiments, although animal experiments undoubtedly throw a considerable amount of light on some of these problems.

Benzene and compounds derived from it are among the most frequent causes of serious disturbances of the blood. All compounds containing the benzene nucleus are now considered potential sources of injury to blood and bone marrow. The site of benzene action appears to be more especially the bone marrow, although action on the circulating elements is apparently also present. In the bone marrow benzene compounds cause structural and functional disturbances of the elements concerned with the formation of the red cells, the white cells and thrombocytes. In the extreme grades of chronic poisoning there is a typical picture of aplastic anemia.

There are conditions, however, under which these substances are much more selective in their action, giving rise, for example, to fairly typical cases of purpura haemorrhagica, in which only the thrombocytic element of the bone marrow is injured; or agranulocytosis, in which specific action on the white cell marrow is produced; or fairly typical pictures of hemolytic anemia, in which the white cells are influenced little if at all. Those are the more infrequent types; nevertheless such selectivity is encountered.

Although the mother substance, benzene, seems to be capable of most of the essential actions on the blood and the blood forming organs, derivatives tend to shift the pattern of actions, bringing out some and suppressing others. Many such examples are found in pharma-

cologic literature, and this phenomenon also is not confined to the pharmacology of the blood. The more important compounds are:

1. Phenylhydrazine and compounds derived from it, antipyrine and aminopyrine.
2. Sulfanilamide.
3. Aniline and its derivatives acetanilid and acetophenetidin.

Phenylhydrazine produces its most striking effect on the red cells, causing hemolysis. A derivative of phenylhydrazine, antipyrine, and another one, aminopyrine, hardly influence the red cells at all but act predominantly on the white cell structures of the bone marrow. Sulfanilamide seems to stand somewhere between those two. It produces hemolytic anemia, a hemolytic action on the red cells, and also agranulocytosis, which appears to be a more or less specific type of action on the myeloblasts, interfering with their maturation. Acetanilid and acetophenetidin hardly influence the bone marrow at all. Their action is exerted chiefly on the hemoglobin. These compounds may give rise to cyanosis resulting from methemoglobinemia and sulfhemoglobinemia.

A review of some of the experimental and clinical literature on poisonings by benzene as well as some of its derivatives, aminopyrine and sulfanilamide, makes possible a certain number of general statements concerning their behavior:

First, individual differences in susceptibility to these compounds are observed. Only rare individuals of a large group that are exposed appear to contract the blood disorder. Perhaps we may discuss the causes of these differences. Do they represent anything fundamentally different from the individual differences in susceptibility that are seen, for example, in connection with morphine, epinephrine or any other drug?

The allergic hypothesis has been introduced into this story. It has been advanced as a mechanism of the action of these compounds. A doctor in whose hands a patient has been poisoned with one of these compounds heaves a sigh of relief when the magic word "allergy" or "idiosyncrasy" is uttered. It seems to free one of responsibility for overdosage. I was particularly struck by a report in which a baby 1 year old received daily doses of 1 Gm. of sulfanilamide for many days. Hemolytic anemia developed. It was ascribed to idiosyncrasy to sulfanilamide. The dose represents the equivalent of about 7 Gm. of sulfanilamide daily to adults, a large dose. Many of the cases appear to represent poisoning by the direct toxic action of the drug rather than to involve any qualitatively peculiar state because the doses of the drug supply a source of benzene equal to the doses of benzene intended for the suppression of bone marrow, as in the treatment of leukemia.

In the course of poisoning, particularly if it involves the bone marrow, as Kracke has pointed out in connection with agranulocytosis, there are three more or less distinct phases. In the more fulminating type these phases are not so distinct, but in the more chronic type they are the bone marrow phase, the blood phase and the clinical phase or the symptom phase. It simply means that there may be a great deal going on in the bone marrow long before one begins to detect changes in the circulating blood. Animal experiments which Dr. Climenko made in this laboratory some years ago have a bearing on this. He gave large doses of cyclic compounds and produced marked changes in the marrow of rabbits while the circulating blood remained normal.

Prolonged exposure to a given concentration of these compounds seems to produce effects which are not seen after short exposure. That is unusual, as drugs go. If one exposes a patient for a long time to a given concentration of quinidine or digitalis, whatever effect has been obtained with that concentration at the beginning continues, but in the case of these compounds the same concentration continued over a long time seems to do something to the bone marrow which is not due to the fact that more drug is accumulating. Specifically, if no toxic effects seem to occur with 5 mg. of sulfanilamide per hundred cubic centimeters of blood in five or six days, does that fact preclude injury if that concentration is continued for thirty or forty days?

When the compounds of the benzene group are discontinued after having been taken for some time, the effects may continue, and several days or even weeks later the manifestations of poisoning may appear.

DISCUSSION OF QUESTIONS

STUDENT: Dr. Gold has suggested that the use of acetanilid and acetophenetidin results in methemoglobinemia and sulfhemoglobinemia. Where is the sulfur derived from for the production of sulfhemoglobinemia?

DR. GOLD: These drugs do not produce methemoglobinemia or sulfhemoglobinemia directly. The evidence at present seems to indicate that in some way they sensitize the hemoglobin to the action of reducing agents or to sulfur compounds. If a large dose of hydrogen sulfide is given to a dog it fails to produce sulfhemoglobinemia, but if that dog has been treated with acetophenetidin daily for several days then the same treatment with hydrogen sulfide will result in sulfhemoglobinemia, although the acetophenetidin itself did not produce it. An interesting contribution to this subject has been made by Snapper in Holland and by Harrop and Waterfield in this country. In regard to methemoglobinemia the view is that reducing substances like nitrites absorbed from the gastrointestinal tract reduce to methemoglobin the hemoglobin "sensitized" by aniline derivatives. These compounds may exert some sort of catalytic action by which the change is brought about.

DR. CARL SMITH: Our dose of sulfanilamide for children is 0.2 Gm. per kilogram, and for a baby weighing about 12 Kg. the dose would be 2.4 Gm. a day. This has proved quite safe in our hands, although a smaller dose daily caused hemolytic anemia in the reported case that Dr. Gold mentioned.

DR. McKEEN CATTELL: It has been reported that relatively larger doses of sulfanilamide must be administered to children in order to obtain a given blood concentration.

DR. WALTER MODELL: Dr. Gold raised the question of the increasing effect of benzene compounds when a fixed dose is given over a long period of time. It has been found in studies on the prevention of relapses in rheumatic fever in children employing about 2 to 5 Gm. of sulfanilamide a day over many months that if there is no evidence of an effect on the bone marrow in a short time the drug can be continued for many months without showing this effect.

DR. CATTELL: It would be desirable to have further discussion on the problem which Dr. Gold raised regarding possible idiosyncrasy to these drugs. Dr. Rhoads has carried on experimental studies on the effects of vitamin deficiencies in relation to susceptibility, and I wonder if he would tell us something about them.

DR. CORNELIUS P. RHOADS: Our observations are still incomplete and wholly inconclusive. We felt that we had clear evidence from animal experiments that in the presence of inadequate diets the effect of aminopyrine on the bone marrow was more pronounced than when adequate diets were fed.

We have been very much interested in the effect of dietary constituents on the conversion of a variety of cyclic hydrocarbons. In the monkey, for example, dibenzanthracene produces not a malignant tumor at the site of injection but a condition similar to aplastic anemia in man. Experiments are in progress to ascertain how this effect can be altered, but we have no conclusive evidence at the present time. I am sure that there is no valid proof at the moment for the participation of dietary constituents in the conversion and supposed detoxification of any of the compounds discussed this morning. It is possible that something of that sort may develop. I think you all know of the observation of Dr. Levine and his co-workers, who have recently shown an improper metabolism of the cyclic amino acids in the presence of vitamin C deficiency. We had already noted a similar occurrence in certain patients with hepatic disease, but we had not ascertained the vitamin C effect.

There is a long story concerning the effect of dietary constituents on susceptibility to the compounds used in the munitions works in the great war. The observation was made, and a very poor and inadequate observation it was, that the effect on hemopoiesis of exposure to trinitrotoluene was most marked in persons who took inadequate diets. There were made at that time certain experiments on rabbits using naphthalene as a toxic cyclic compound. It was shown that the toxic effect could be inhibited by giving adequate diets and was more marked when inadequate diets were fed. That observation led to the work of Bourne, who showed that naphthalene cataract could be prevented by feeding diets high in cysteine, and to a series of experiments concerning the participation of cysteine in the detoxification of various cyclic compounds.

Goerner observed that the toxic effect of dibenzanthracene was much more marked when the animals were on a deficient diet, and that observation we have confirmed. Furthermore, we have some evidence, but wholly inconclusive, that the conversion of dibenzanthracene into dihydroxydibenzanthracene is conditioned to some extent by something in the diet.

I regret that I have to be so indefinite, but I have been at this for a good many years, and still we don't have accurate methods; hence absolute proof is not at hand.

DR. CATTELL: Would you say something about those indole experiments in anemias?

DR. RHOADS: If dogs are fed a normal diet with a high content of meat and given about a gram of indole a day the drug is tolerated without considerable anemia, though the animals vary in their susceptibility, and some increase in the output of bile pigment can be demonstrated as evidence of blood destruction. The rate of blood destruction caused by the indole given with a normal diet is not sufficient to produce anemia of any considerable degree, and what little is produced is compensated for by increase of active marrow. If the animals are starved or fed a diet lacking something contained in yeast or liver and then given indole, a pronounced anemia is produced very rapidly with or without marked increase in numbers of reticulocytes. If the diet is made normal once more, the blood levels

will rise rapidly, though they will not always come back to normal. It seems to us that by lack of a dietary constituent—and we have never identified it, there may be more than one—the susceptibility of the animal to the hemolysis by indole was increased, and that susceptibility could be overcome by making the diet normal.

Those experiments were checked in a second series with sterile biliary fistulas so that the excretion of bile pigment could be measured. The results were corroborative; that is, the hemolysis was active while the diet was bad and less active when the diet was good.

DR. DAVID R. CLIMENKO: I think one of the things you should bring in is the possible mode of action, Dr. Rhoads, and speak of your *in vitro* work on the hemolytic action of indole as against indican.

DR. RHOADS: That work was done by Dr. Ponder in collaboration with us. Dr. Ponder showed that indole *in vitro* in sufficient concentrations is lytic to normal red cells, and that the normal conversion product of indole, indican, is not lytic. That observation is easily reproduced, and I think there is no question about it. We inferred of course that the conversion of indole to indican in our dogs was interfered with in the presence of the poor diet, but we have not been able to prove that. We could not demonstrate any difference in the blood levels of indole or indican in animals on good or poor diets, so I am not at all sure that this matter of conversion of hydrocarbons is at all settled. It is a terribly difficult one. We have studied the glycuronide and sulfate mechanisms in patients and we are now studying the hydroxylation, but we still have no conclusive experiments. It is worth while to mention the studies on butter yellow although they do not bear on the blood dyscrasies. Several Japanese workers administered alpha-amino-azotoluene and also aminoazobenzene to animals. Both of these agents are destructive to liver tissue, and liver cancer will result. The effect will occur, however, only if the animals are fed an inadequate diet, and the animal is entirely protected if the diet is adequate. We do not know the constitution of the dietary substance, but the fact is clear that the destructive effect of these two compounds is seen only when the diet is inadequate and is never seen if the diet is made adequate. I think that is in some sense a confirmatory thesis, that there may be a detoxification mechanism controlled by some constituent of the diet.

HEMOLYTIC ACTION OF SULFANILAMIDE

DR. CATTELL: Are there questions for Dr. Rhoads? If not, perhaps Dr. Climenko would make a few remarks on the hemolytic action of sulfanilamide.

DR. CLIMENKO: I should like to bring out one point regarding the possible mode of action of sulfanilamide as an etiologic agent in the production of hemolytic anemia. If one makes a normal time kinetic curve for the action of lysin on normal red cells, one gets a fairly definite curve and finds a definite relation between time required for total lysis and concentration of lysin. If one adds to such a system a quantity of sulfanilamide such as is ordinarily present in the blood in therapeutic ranges, approximately 10 mg. per hundred cubic centimeters, the curve will be altered in this manner: the action of the lysin on these cells will be accelerated. The cells are less resistant to the lytic agent than they were before the addition of sulfanilamide. It should be pointed out that aniline, for example, possesses the same accelerating effect to a more marked degree.

In the body, aniline goes through this probable mechanism: It is converted from aniline to phenylhydroxylamine and from phenylhydroxylamine to par-aminophenol. A large portion of it is excreted in the form of a conjugated ethereal sulfate. It has been shown that following the administration of aniline or benzene there is an increased output of ethereal sulfates in the urine.

We have found that this holds true in the case of sulfanilamide. The ratio of ethereal sulfates to inorganic sulfates present in the urine after the administration of sulfanilamide will be increased. Most of the sulfanilamide that is administered can be recovered either as sulfanilamide or as acetyl derivative. A small proportion of it—less than 5 per cent—cannot be accounted for. From our indirect evidence on the increased output of ethereal sulfate after the administration of sulfanilamide, it may be suggested that a small proportion of the drug goes through this oxidation mechanism, and, as it may occur to a greater extent in certain individuals than in other individuals, it may be suggested as a possible explanation for the occurrence of the blood dyscrasias which arise in the so-called "susceptible" individual.

DR. GOLD: As to the increase in susceptibility of the cells to lysis, is it also true about cells taken from the blood after sulfanilamide has been given?

DR. CLIMENKO: Unfortunately the reverse is true. There is an increase in the resistance of the cells to the lytic agent. This occurs some days after the administration of sublethal doses of benzene or aniline. The explanation may be that the less resistant cells have already disappeared as a result of an acceleration of the normal lytic mechanism in the body, and that the *in vitro* hemolytic system is made up only of the more resistant cells which are still present in the circulation.

DR. GOLD: Here is an interesting point. It comes up in connection with many drugs which destroy the blood cells: Alcohol, which causes some lysis of blood cells after prolonged administration, will also leave the blood more resistant to lytic agents, and a similar resistance develops after phenylhydrazine. After it has lowered the red cell count, a degree of resistance to further lowering is noted. The cause of this resistance is probably the fact that the population of red cells which survives is a hardier population.

DR. CLIMENKO: I think that is probably the explanation.

EFFECT OF METALS

DR. CATTELL: Dr. Reznikoff will discuss the effect of metals, especially lead.

DR. PAUL REZNIKOFF: I may first say a few words about gold salts. These depress any or all of the constituents of the bone marrow. Another characteristic of gold which I should like to emphasize is that it is stored and its effects may be present a long time after the gold is administered. We had a nurse who was given gold therapy for lupus five years before she injured her foot. She had an infection following the injury, and after this mild infection there developed an aplastic bone marrow involving all of the elements. I bring that up because gold is used in the therapy of lupus and is now also being used for arthritis. So let us watch out for gold salts.

I wish to speak briefly about the action of lead on the red blood cells. *In vitro*, lead salts cause the erythrocytes to shrink and become rigid so that they cannot swell and shrink as readily as normal cells.

They become brittle and more fragile to trauma. These "leaded" cells tend to clump and their specific gravity increases. If normal red blood cells are placed in modified Ringer's solution the salt content of which varies from 0.5 to 1.3 per cent, the specific gravity of the cells varies from 1.060 to 1.110. Under the same conditions "leaded" erythrocytes seem heavier, the range being from 1.082 to 1.111. The behavior of lead red blood cells in hypotonic saline solution (fragility test) is also interesting. In the more dilute solutions (from 0.15 to 0.3 per cent) these cells hemolyze less readily, probably because they are more rigid. However, in the zones from 0.4 to 0.5 per cent they tend to break up more readily. This phenomenon can be duplicated *in vivo* if 1 Gm. of a lead salt is given to a rabbit by mouth and its blood is tested.

Lead salts cause anemia by hemolysis. The affected cells cannot withstand the trauma of circulation and the swelling and shrinking when changing from the venous to the arterial systems as readily as normal erythrocytes. The so-called stippled cells are really reticulocytes the reticulum of which has become discrete or punctate. These are increased in number because of the reaction of the bone marrow to hemolysis. A reticulocyte count, in my opinion, is a much more delicate index of the action of lead on the red blood cells in the circulation than the count of the stippled cells.

The anemia of lead poisoning usually takes care of itself if the lead is removed from the circulation. Neither iron nor liver extract is indicated. In the severe anemias transfusions are the only means of bringing the blood count to a normal level, just as in any other hemolytic anemia.

There are two schools of thought concerning the treatment of lead poisoning after the acute symptoms have subsided. One group tries to delead the patient by putting him on a low calcium diet (0.2 Gm. a day) and administering ammonium chloride in about 4 Gm. doses daily for a few days. This produces an acidosis and the patient excretes more lead. Another method, and I follow this plan with my patients, is to store the lead in the bones by giving a high calcium intake and vitamin D. As long as lead is removed from the circulation and stored in the bones, it is harmless. Of course, the symptoms and signs of lead poisoning, such as colic, palsy and encephalopathy, have to be treated individually. For the details of the therapy of lead poisoning, I refer you to chapter 15 in a book which has just been published by the Oxford University Press entitled "Industrial Hygiene," edited by Lanza and Goldberg.

TREATMENT OF DRUG DISORDERS

DR. CATTELL: Dr. Forkner, will you describe the management of patients who show evidence of disorders of the blood due to a drug?

DR. CLAUDE S. FORKNER: Frequently patients will not be aware that they have taken any harmful drugs. This information must be obtained by careful detective work. At times remaining samples of the drug can be supplied by the patient or a prescription can be traced. The effects of drugs harmful to the blood-forming organs are not infrequently delayed for several days, several weeks or even months. The most important point in treatment is to discontinue any medication which may be suspected as the offending agent. Thereafter symptomatic treatment is indicated, with careful attention to the behavior of the number and quality of the structural elements of the blood. If severe bleeding, the result of thrombocytopenia, is present, frequent

transfusions of blood may be necessary. Severe anemia also may require blood transfusions. Careful attention to the oral hygiene may prevent ulceration of mucous membranes. A well balanced nutritious diet with added vitamins should be given. The object of the treatment is to support the patient until the body has had opportunity to destroy or eliminate the drug and regain normal function.

BLOOD DISTURBANCES FROM SULFANILAMIDE

DR. CATTELL: When blood disturbances develop in the course of treatment with sulfanilamide and its derivatives, what are the criteria for deciding whether or not to continue the treatment?

DR. FORKNER: Under such conditions one must try to determine whether the effects are due to the drug or to the disease itself. Usually if acute hemolytic anemia or acute agranulocytosis occurs, the drug should be discontinued promptly and not resumed. It is important to make blood counts frequently in cases in which sulfanilamide derivatives are being administered. A differential count and a red blood cell count are the most important parts of the study, since they may change in an unfavorable direction before the total white cell count or hemoglobin values are altered significantly. A marked drop below normal in the percentage of neutrophils or a sharp fall in the red blood cell count is a danger signal. The appearance of jaundice, the result of hemolysis, or ulceration of the mucous membranes, the result of agranulocytosis, usually means that the process is well advanced. These signs may be avoided in some cases if careful attention has been focused on the percentage of neutrophils and the total number of erythrocytes during the course of treatment.

DR. JANET TRAVELL: Do barbiturates containing a ring nucleus, like phenobarbital, injure the blood?

DR. GOLD: Phenobarbital has been included among agents causing agranulocytosis. There is little doubt about its potentiality in that direction by reason of its ring formation, but the evidence that such effects have been produced is not satisfactory.

SUMMARY

DR. CATTELL: The blood and the blood forming organs exhibit a special susceptibility to foreign substances. Toxic effects have been reported for the greatest diversity of chemical agents, effects which simulate most of the known disorders of the blood. A striking characteristic of poisoning of this nature is great difference in individual susceptibility, and because a widely used drug only occasionally gives rise to blood dyscrasias the affected person is usually regarded as having an "idiosyncrasy" toward that drug. It is questioned whether this represents a qualitatively different reaction, for those individuals may be at the end of the scale of a wide distribution curve.

It appears that there is but meager knowledge of the mechanism concerned in the blood changes produced by drugs, or of the conditions which determine special susceptibility. It has been observed experimentally that deficient diets increase the toxicity of various drugs, and there is evidence that in some instances this is related to vitamin intake.

The problem is important from the standpoint of industrial toxicology and of the therapeutic administration of drugs, and because it complicates the picture from a diagnostic point of view. In treatment the dangers of toxic manifestation from a drug must be weighed against its therapeutic value. The primary consideration

in treatment is the early recognition of the blood changes so that the offending drug may be discontinued or the patient removed from the source of poisoning. Treatment is almost entirely symptomatic and has as its objective the support of the patient until the body has had opportunity to eliminate the drug and regain normal function. The most important single measure is transfusion. A well balanced, nutritious diet should be given, and added vitamins are probably of value. In cases of chronic lead poisoning it is not recommended that the patient be delead but rather that storage of lead in the bones be promoted by giving a high calcium diet and vitamin D.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE.

THE COUNCIL DESIRES TO EXPRESS ITS APPRECIATION TO DR. R. R. NEWELL FOR THE PREPARATION OF THIS ARTICLE AND TO THE CONSULTANTS ON ROENTGEN RAYS FOR THEIR ASSISTANCE. THE CONSULTANTS ON ROENTGEN RAYS ARE DRS. A. U. DESJARDINS, CHAIRMAN, WILLIAM E. CHAMBERLAIN, A. C. CHRISTIE, E. C. ERNST, GIOACHINO FALLA, T. A. GROOVER, F. M. HODGES, G. W. HOLMES, J. T. MURPHY, R. R. NEWELL, E. P. PENDERGRASS, U. V. PORTMANN, L. S. TAYLOR AND J. L. WEATHERWAX.

HOWARD A. CARTER, Secretary.

COUNCIL INSPECTION OF ROENTGEN RAY APPARATUS

R. R. NEWELL, M.D.

SAN FRANCISCO

The Council on Physical Therapy has long considered the practicability of investigating roentgen apparatus. The radiologists asked by the Council to serve as consultants in considering this question are of the opinion that, while there is no gross imposition on the part of American manufacturers of roentgen apparatus against which radiologists need protection, there are many dangers connected with the use of roentgen apparatus by physicians who know very little about it. The following statements summarize the opinions of the consultants:

Modern "shock-proof" and "ray-proof" roentgen ray apparatus is available in a size and at a price that makes roentgenoscopy and roentgenography attainable for almost any doctor. The trained radiologist has sufficient knowledge of the physics and engineering of his specialty to protect himself (if he will) against poor equipment made by a careless or incompetent manufacturer. However, the physician not so trained may need protection by official inspection of apparatus advertised for sale.

It may be true that a physician not having enough training in radiology to conduct his own inspection should not be using a roentgen unit. It may also be true that, instead of having the manufacturer submit the apparatus for Council investigation, the physician who will use the unit might well submit himself to the American Board of Radiology for examination. Nevertheless, to blurt out these truths to a physician who asks the Council for guidance might only serve to hurt his feelings. It would not offer a solution to the practitioner in a small town who wishes to give his patients the benefit of roentgenology as well as the benefits of surgery, otology, dermatology, ophthalmology and all the other specialized skills and knowledge medi-

Dr. Groover died April 20, 1940.

From the Department of Radiology, Stanford University Medical School.

cine is developing—as far as he can master them, when consultation is not available.

If the Council should undertake investigation of roentgen units, limited perhaps to mobile or portable units designed for practitioners who do little radiology, some assurance could be given the purchaser concerning the following necessities:

- (a) Electrical safety:
 1. Grounding of case of transformer, control and tube holder, and grounded sheath to high tension cables.
 2. Absence of excessive leakage in the insulating materials.
 3. Proper circuit-breakers and/or fuses against overloads.
- (b) Ray protection conforming to National Bureau of Standards Handbook 20. There is a special danger in the small apparatus, lest the tubeholder be in contact with patient or nurse. Leakage of ray must be less than 5 per cent of the 50 cm. beam intensity at all places where a hand can be put (outside the cone), as well as being less than 10^{-5} roentgens per second at all points 1 meter distant.
- (c) Assurance that the machine gives the quantity and quality of roentgen rays represented.
- (d) For oil-filled roentgen ray apparatus, assurance that expansion chambers are sufficient to take up heat expansion of the oil without production of bursting pressures (maximum kilovolt, milliamperage and time being labeled on the case).
- (e) A switch requiring to be held on during the exposure, so as to eliminate the possibility of the tube's being left turned on indefinitely.
- (f) An arrangement to prevent roentgen rays being produced, or at least getting out, except when a cone for say 10 inches minimum target-skin distance is attached.
- (g) A 2 millimeter aluminum filter fixed in place (or sufficient added to window, oil, and so on, to give half value layer at least 2 millimeters of aluminum).

Even with these precautions, it is impossible to prevent an inexperienced doctor from burning himself or his patient, as many have done in the past. There is grave question in my mind whether the assurance given by Council acceptance may not prove rather productive of danger than of safety.

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

HOGAN #8870 BREVATHERM ACCEPTABLE

Manufacturer: McIntosh Electrical Corporation, Chicago.
The Hogan #8870 Brevatherm is recommended for medical and minor surgical diathermy. The unit is mounted in a polished wood cabinet which provides storage space in the lower portion. The cabinet size is 44 inches high, 22 inches wide and 16½ inches deep. The weight of the complete unit is 127 pounds.

The wavelength is 12 meters, the frequency 25 megacycles, the oscillator circuit two tubes, tuned grid, tuned plate, push-pull, the plate supply a full wave rectified current. The tubes consist of two 866-A rectifier and two HF-175 oscillator tubes. Three pairs of outlets are marked as follows: "Diathermy and Surgery," "Air-Spaced," "Cable." The diathermy outlets are used for pad techniques and minor surgery. Inductive coupling is used for pads and air-spaced electrodes, capacitative coupling for the cable.

The power and oscillatory plant is enclosed in metal; the firm claims that this feature decreases the radiation of high frequency power from the oscillatory circuit. A ground connection on the back of the unit is provided to ground the metal housing. The firm states that provisions for minimizing radio interference are made.

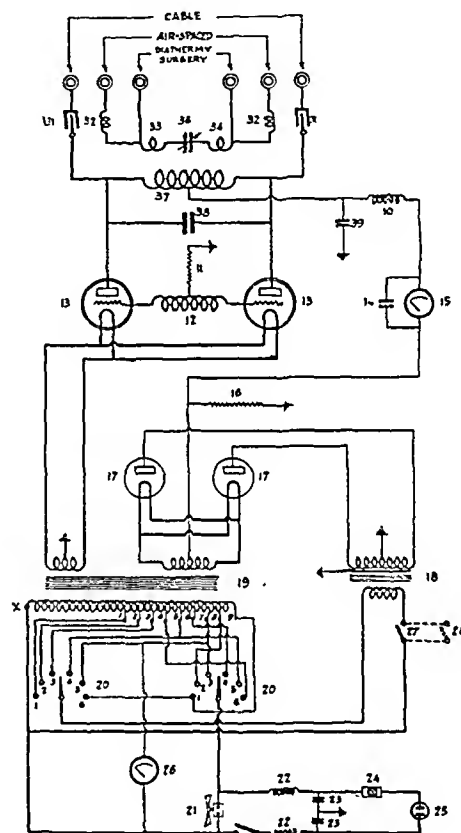
To prevent high frequency energy from entering the power line, the firm states that an extra line filter system of choke coils and filter condensers is built into the apparatus.

An exhaust fan provides forced draft ventilation. By means of an autotransformer and tap switch, line voltage adjustment

can be made to suit voltages varying from 90 to 135 volts. This feature makes it possible for full output to be derived at high or low line voltage conditions. Correct line voltage is indicated by a voltmeter on the panel.

The dosage in the patient's circuit may be regulated by the power output control switch. Six steps of voltage are delivered to the plate circuit of the tubes. The milliammeter employed on the Brevatherm registers the amount of direct current milliamperage which is delivered to the plate of the power tubes. A treatment timer regulates the duration of treatment from zero to sixty minutes.

The #8870 Brevatherm may be supplied with treatment arms and air-spaced electrodes. Each treatment arm has four friction joints; two joints of the friction ball type are self supporting and the other two are manually adjusted with knobs. The arms are constructed of insulating material containing jacks to



Schematic diagram of circuit.

hold cord tips of air-spaced electrodes in position when these are not in use. A cord clamp maintains the alignment of the cord during treatment. The lower metal portion of the treatment arms is grounded to the chassis to prevent pickup of electrical energy from the metal. A neon bulb surmounts each treatment arm and indicates when the circuit is tuned to resonance.

For use in surgical diathermy, a foot switch receptacle is located at the rear of the apparatus; the foot switch cord is also shielded and grounded to the metal chassis.

Evidence for deep tissue temperature measurements was submitted by the firm for the Premier Model superseded by the #8870 Brevatherm, which has a similar circuit. The firm claims the output of the unit to be 500 watts; tests conducted by the Council found a 490 watt output. This discrepancy is within the limits of experimental error. The temperature of the transformer operating on this load came within the requirements of the Council. The Council's clinical investigation of the apparatus revealed that the apparatus gave satisfactory clinical service.

The Council voted to accept the Hogan #8870 Brevatherm for inclusion on its list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, AUGUST 3, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

ACCURATE BLOOD TESTS FOR SYPHILIS

More and more states are passing laws requiring premarital examinations. Twenty of these laws require a physical examination of both sexes as well as blood tests for syphilis. Antepartum examination laws requiring serologic tests have been enacted in eighteen states. The passage of these laws is an important step in the control of syphilis. However, the effectiveness of their application depends on the reliability of the serologic tests employed in making or ruling out a diagnosis of syphilis.

The physician who makes the examination is held responsible for the decision made in the case even though the basis for his diagnosis may rest largely on the results of serologic studies. This fact makes it necessary for him to know the accuracy of such serodiagnostic tests.

Serodiagnostic evaluation studies carried out during the last four years by the U. S. Public Health Service and state departments of health have shown conclusively that many laboratories have not met the minimum standard of efficiency of serologic test performance.

An assembly of laboratory directors and serologists which was attended by representatives from state, municipal and private laboratories was held in Hot Springs National Park, Ark., in October 1938. This meeting was sponsored jointly by the Committee on Evaluation of Serodiagnostic Tests for Syphilis and the U. S. Public Health Service. The representatives who attended this meeting agreed that a satisfactory serologic test for syphilis is one which has a specificity rating of at least 99 per cent and a sensitivity rating not more than 10 per cent below that of the test as performed simultaneously by the author or control serologists. This definition is arbitrary, but any definition of a satisfactory test must necessarily be arbitrary at this time. The present conception of a satisfactory test is, however, believed to be reasonable.

The first serodiagnostic evaluation study, made in 1937, showed that many laboratories of the country were operating at a questionably satisfactory or totally unsatisfactory level of efficiency with regard to sensitivity and specificity. In 1938 the results reported by ten state laboratories closely approximated the results of the control laboratories, and five additional laboratories reported results which were considered satisfactory. The performance of one or more tests in thirty states, however, was unsatisfactory.

In the 1939 investigation three state laboratories reported results comparable to those of the control laboratories. This number was in addition to the ten laboratories whose performance was comparable to the control laboratories in 1938 but which did not participate in 1939. Thirteen additional laboratories did satisfactory tests, but the performance in one or more tests in twenty-three laboratories was unsatisfactory.

These studies show gradual improvement in the efficiency of many state laboratories, but the level of efficiency of local laboratories which perform serologic tests in many states is as yet undetermined. Studies of the efficiency of serologic test performance such as those conducted by the Committee on Evaluation of Serodiagnostic Tests for Syphilis offer the only practical means now known to determine the comparative efficiency of each laboratory. The physician who considers the welfare of his patients will insist that the laboratories in his state participate in well organized performance studies. Every physician should know the sensitivity and specificity rating of the laboratory to which he sends his specimens.

Physicians should not be satisfied with a satisfactory rating of the state health laboratories alone but should demand intrastate studies of the performance of serologic tests in municipal, hospital and private laboratories. After a state laboratory has been rated as satisfactory,

it is in a position to act as a control laboratory for intrastate studies of other laboratories. It should also be in a position to advise and assist other laboratories in bringing their efficiency up to an acceptable standard and to maintain this standard once it has been reached.

If the laboratories within a state are rated according to the efficiency of the test performed as superior, satisfactory or unsatisfactory, the physician will be able to choose a laboratory on which he can safely rely. At present, under the new premarital laws, few states will accept the reports of serologic tests performed in other states because the efficiency of the serologic work is unknown. The evaluation and rating of laboratories in the various states should eventually result in the reciprocal acceptance of the reports of serologic tests performed in other states.

Support by the medical profession of this attempt to improve the performance of serologic tests for syphilis will not only aid in the better administration of the various laws pertaining to the control of syphilis but will also serve as a stimulus to the improvement of serodiagnostic methods throughout the country. For the first time in the history of the United States it is possible for laboratories to ascertain the reliability of their serologic test performance not only on the basis of comparison of results in different laboratories but also on the basis of serologic results as contrasted with the known clinical diagnoses of the donors of the specimens.

DOUBLE BARRELED SELF MEDICATION

Even the old Food and Drugs Act required declaration on the label of the amount of acetanilid in a remedy. As a result some, but not all, manufacturers replaced acetanilid with acetophenetidin (phenacetin), acetylsalicylic acid and other drugs. Now comes the new Food, Drug and Cosmetic Act, which requires declarations of all active ingredients. Furthermore, this legislation requires the declaration of the amounts of some drugs, and included in this list are both acetanilid and acetophenetidin. A number of preparations on the market have combined the "virtues" and, more significantly, the dangers of acetophenetidin and significant amounts of bromides. Such preparations are doubly dangerous; they accustom the user to the taking of bromides and thus insure a continued dosage of acetanilid. The results in some cases have been disastrous. Unlike the old act, the new Food, Drug and Cosmetic Act requires qualitative and quantitative declaration of the presence of bromides. Thus the new act has clearly indicated that these drugs are sufficiently potent to require quantitative declarations on the label. There is, however, a stipulation in the new act which has been considered to be applicable to such a combination when it is promoted directly to the public. Quoting from the new act:

Sec. 502. A drug or device shall be deemed to be misbranded—(j) If it is dangerous to health when used in the dosage, or with the frequency or duration prescribed, recommended or suggested in the labeling thereof.

A release of the United States Department of Agriculture dated March 28, 1939, included the following sentence:

Actions against drugs alleged to be dangerous and to violate the new law included 3 bottles of Cal-Co-Din, a pain-killer containing cinchophen; 488 packages of B. C. Headache Powders, 11,325 bottles of Bromo-Seltzer, and 3,526 packages of Stanback Headache Powders, all of which contained, among other ingredients, bromides and acetanilid.

It is noteworthy that the seizure of BC Headache Powders referred to above has resulted in a Notice of Judgment being issued on the basis that the powders "would be dangerous to health when used in the dosage or with the frequency or duration prescribed, recommended or suggested in the labeling," and because the "labeling failed to reveal facts material with respect to the consequences which might result from the use of the article under the conditions of use . . . and failed to bear warnings against use in pathological conditions where its use might be dangerous to health or against unsafe dosage or duration of administration." The company was granted a petition to withdraw its claim and answer. Judgment of condemnation was entered and the product was ordered destroyed.

In a circular letter addressed to a layman, the manufacturer of "BC" Headache Powders suggests the use of this remedy for the relief of pain and discomfort due to headache and neuralgia. It is also claimed to be effective for the relief of muscular aches, discomforts due to simple head colds, and as a sedative in "simple nervousness." This letter was received quite recently. Enclosed in the letter was a sample which contained such warnings as "May be repeated in 3 or 4 hours. Do not use more than two powders in any 24-hour period. Not for use by children." And finally, "When pains of this character persist, or recur frequently, consult a physician." Possibly these warnings would be interpreted to mean that the use of the preparation should not be continued or repeated. The warnings become less effective, however, when the advertising contains such statements as "The test of time (30 years) and the distribution of millions of packages have established the merit of 'BC' and gained for it the whole-hearted acceptance on the part of many people in all parts of the nation."

Drugs like acetanilid and the bromides are useful when prescribed by the physician in an individual case to meet certain immediate requirements. Such use is not comparable to promiscuous use by the layman. Useful Drugs, a publication addressed to physicians, states with regard to acetanilid:

In poisonous doses acetanilid produces cyanosis, an abnormal reduction of temperature, coldness of the extremities and profuse sweating. In individuals with an idiosyncrasy toward the drug similar symptoms may be produced by small doses. It should be avoided or used cautiously in patients who are debilitated from any cause, especially those with heart disease. Acetanilid is effective for the relief of headache, neuralgic pain, and for the aches and pains of the febrile patient, but is not suited to the treatment of pain caused by inflammation. It has

been exploited widely as a universal analgesic in various mixtures and under different names. Many so-called headache powders contain it; its indiscriminate use in such forms is dangerous.

Dosage: 0.2 Gm. (3 grains). It is well to begin with 0.1 Gm. (about 1½ grains), and to repeat cautiously.

Note that it is suggested that the physician start with 1½ grains. These manufacturers start patients about whose physical condition they know nothing with 2½ grains. Useful Drugs also says concerning potassium bromide:

Actions and Uses: Potassium bromide is a sedative for the nervous system. It diminishes reflex excitability and depresses the motor area of the cortex. In large doses it is depressant to the circulation. When continued long it disturbs the nutrition and may produce irritation of the skin similar to that produced by the use of iodides.

It is to be emphasized that these cautions are for the proper and scientific use of these drugs when they are employed by physicians. THE JOURNAL continues to insist on the danger of placing preparations containing such drugs in the hands of the public. However thoroughly labeled, such a double barreled instrument of self medication represents infinite potentialities for harm through promiscuous use by the uninformed lay person.

Current Comment

CONSULTATION SERVICE BY MAIL

A recent opinion by the department of justice of Pennsylvania, published in the July issue of the *Pennsylvania Medical Journal*,¹ provides an interesting point of view regarding medical consultation by mail. In 1939 a Pennsylvania law was passed requiring an applicant for a marriage license to submit a statement from a duly licensed physician of the commonwealth certifying that the applicant is not infected with syphilis or, if infected, is not in a stage of the disease which is likely to become communicable. Any applicant having been denied a physician's statement may appeal to the department of health for a review of his case and the department may, after appropriate investigation, issue or refuse to issue a certificate in lieu of the required physician's certificate. To facilitate the review of such a case on appeal, the department of health proposed to utilize the facilities of the Institute for the Control of Syphilis of the University of Pennsylvania. This institute, it was contemplated, would be supplied with a statement of facts embodying the history of the applicant's case, his present physical condition, the results of serologic tests and other pertinent information. Solely on the basis of this statement, it was proposed, the institute would advise the department of health what action to take on the appeal. It was not contemplated that the applicant should be examined by members of the institute. The department of health further proposed, as a part of its venereal disease

program, to make the services and facilities of the institute available to licensed physicians throughout the commonwealth for the purpose of consultation. It seems to have been the plan that any physician treating a person suspected of being infected with syphilis might submit to the institute a statement of the case and obtain a recommendation as to diagnosis and a proper course of treatment. Before the plan was put in operation, however, the department of health submitted it to the Pennsylvania department of justice, asking specifically whether the director or any individual member of the institute would incur civil liability "for giving advice by correspondence regarding the care of, or prescribing treatment for, a patient he has never seen or examined, if the advice actually results in unfavorable or injurious consequences to the person regarding whom it was given." The resulting opinion, formulated by Deputy Attorney General Fred C. Morgan, answers the question in the affirmative. While, the opinion points out, the identical question at issue had never been adjudicated in the commonwealth, the general principles applicable to the relationship between a physician and his patient clearly lead inevitably to the conclusion reached. Consultation among physicians is common practice but almost invariably the consultant is afforded the opportunity to and does examine the patient before making a diagnosis or suggesting treatment. To follow any other practice is to depart from the accepted procedure. The opinion points out that the Principles of Medical Ethics of the Association with respect to consultations obviously contemplate a personal relationship based on a physical examination by the consultant. The Judicial Council has repeatedly condemned as unethical the physician who without seeing a patient attempts to diagnose and to prescribe treatment by mail. After reviewing a number of court decisions involving analogous issues, the opinion concludes:

We have concluded that no physician, and particularly no expert, is entitled, under the law, to rely on the diagnosis of such a serious disease as made by another physician; that he cannot, with impunity, make a diagnosis or suggest indicated therapy for a patient he has never physically examined. The technic of diagnosis is too difficult, the ramifications of the disease too complex. From a study of the foregoing authorities, as well as from considerations of sound public policy and the rationale of malpractice liability, we believe that a consultant who does not personally confer with and examine a patient accepts at his peril statements and reports made to him by the attending physician. To hold otherwise would be to relieve the consultant of his burden to exercise the due care and diligence required of him by law; under such circumstances "due care" certainly contemplates and requires a diligent oral and physical examination of the patient. This is particularly true when the consultant, an expert in a particular field, relies on the observations and findings of one who is not a specialist.

We are of the opinion, therefore, and you are accordingly advised that the members of the Institute for the Control of Syphilis of the University of Pennsylvania would be liable for damages in an action of trespass for malpractice for making a diagnosis of, or prescribing treatment for, a patient they have never seen or examined, if such diagnosis or advice actually results in injurious consequences to the person regarding whom it was made or given.

1. Diagnosis or Treatment in Absentia Not Good Medical Practice, *Pennsylvania M. J.* 43:1473 (July) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

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Journal of the American Medical
Association

* Deceased.

COMMITTEE ON MEDICAL PREPAREDNESS

This committee was created by the House of Delegates of the American Medical Association to cooperate with the Advisory Commission on National Defense, the Army and Navy Medical Corps, the United States Public Health Service and all other federal agencies in preparing our nation medically to meet any emergency. The functions of the Committee include the following activities:

1. Meetings devoted to consideration of problems involved in providing medical personnel for military, naval and civilian needs.
2. Consideration of the provision of medical personnel for physical examination, particularly of young men who are conscripted for medical service, young men assigned to vocational training, persons on relief and those concerned with war industries.
3. Consideration of economic problems including financial arrangements, leaves of absence, part-time service and other factors associated with civilian medical services.
4. To maintain contact and to represent the Association in conferences with the Surgeon Generals of the Army, Navy and Public Health Service and, when necessary, with other governmental agencies.
5. To maintain contact with the state chairmen on medical preparedness.
6. To encourage and coordinate the activities of the various state chairmen for the National Committee on Medical Preparedness.
7. To formulate instructions for the guidance of state chairmen.
8. To review and to approve or disapprove recommendations received from state chairmen.

Activities of State Chairmen and Committees on Medical Preparedness

The functions of the state chairmen for the state committees on Medical Preparedness are an extension of the functions initiated and developed by the national committee. The National Committee on Medical Preparedness includes representatives located in all of the various Army Corps areas and Naval districts. The state chairmen for the Committee on Medical Preparedness maintain contact with other state chairmen in their vicinity through the corps area representative of the national committee and maintain contact also with the

headquarters office of the American Medical Association, which acts as headquarters for the National Committee on Medical Preparedness.

The functions of a state chairman include the following:

1. Contact with and coordination of the activities of state, county and district medical societies.
2. Cooperation with county medical societies in securing completion and return of the questionnaire on personal information.
3. To establish mechanisms for securing supplementary information to the questionnaire when necessary.
4. To organize a state committee on medical preparedness to be composed of the president and the secretary of the state medical society, the state chairman for the Committee on Medical Preparedness and ex officio the member of the Committee on Medical Preparedness of the American Medical Association within whose corps area the state is located and such other members as this group may select.
5. To assist in the organization of county committees on medical preparedness.
6. To invite local and state health authorities to participate in the work of the program particularly in the matter of civilian health.
7. To arrange for the dissemination of information on medical preparedness to the groups that are concerned with any particular matter.
8. To assist in the verification of the qualifications of physicians desired for service in the Army, industry, special physical examinations and other special work necessary for national defense.
9. To report to the Committee on Medical Preparedness a list of the names of physicians from each county of the state whose services are believed to be necessary for the maintenance of civilian health and who should, in the opinion of the state committee on medical preparedness, be exempt from military service.

State Chairmen

ALABAMA.—Dr. J. N. Baker, 519 Dexter Avenue, Montgomery.
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ARKANSAS.—Dr. W. R. Brooksher, 602 Garrison Avenue, Fort Smith.
CALIFORNIA.—Dr. Philip K. Gilman, 2000 Van Ness Avenue, San Francisco.
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NEW YORK.—Dr. Samuel J. Kopetzky, 71 East Eightieth Street, New York.

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OHIO.—Dr. Harry V. Paryzek, 25 Prospect Avenue N. W., Cleveland.

OKLAHOMA.—Dr. Henry H. Turner, 1200 North Walker Street, Oklahoma City.

OREGON.—Dr. Charles E. Hunt, 132 East Broadway, Eugene.

PENNSYLVANIA.—Dr. Charles H. Henninger, 500 Penn Avenue, Pittsburgh.

RHODE ISLAND.—Dr. Halsey De Wolf, 199 Thayer Street, Providence.

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SOUTH DAKOTA.—Dr. William Duncan, Webster.

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TEXAS.—Dr. Holman Taylor, 1404 West El Paso Street, Fort Worth.

UTAH.—Dr. John F. Sharp, 75 South Main Street, Salt Lake City.

VERMONT.—Dr. Benjamin F. Cook, 46 Nichols Street, Rutland.

VIRGINIA.—Dr. Hugh H. Trout, 1301 Franklin Road, Roanoke.

WASHINGTON.—Dr. Raymond L. Zech, 509 Olive Way, Seattle.

WEST VIRGINIA.—Dr. Benjamin H. Swint, 240 Capitol Street, Charleston.

WISCONSIN.—Dr. R. E. Fitzgerald, 2750 North Teutonia Avenue, Milwaukee.

WYOMING.—Dr. George H. Phelps, 1606 Capitol Avenue, Cheyenne.

ALASKA.—

CANAL ZONE.—

HAWAII.—

PHILIPPINE ISLANDS.—

PUERTO RICO.—Dr. O. G. Costa-Mandry, Department of Health, San Juan.

STATE SOCIETY CREATES MEDICAL PREPAREDNESS COMMITTEE

A Committee on Medical Preparedness, composed of eight New Jersey physicians, has been appointed by the Medical Society of New Jersey to assist the National Committee on Medical Preparedness appointed by the American Medical Association.

Members of the New Jersey committee are Drs. Charles H. Schlichter, Elizabeth, chairman; Harold D. Corbusier, Plainfield; Albert G. Hulett, East Orange; Andrew F. McBride, Paterson; David A. Kraker, Newark; Wells P. Eagleton, Newark; David B. All-

man, Atlantic City, and Thomas K. Lewis, Camden. Dr. Norman M. Scott, 143 East State Street, Trenton, is secretary to the committee.

The purpose of these committees—state and national—is to determine by a survey the professional facilities available for a successful medicomilitary program which will at the same time assure continuity of adequate medical care for the civilian population during any national emergency.

A questionnaire form has been sent directly to each physician in the United States by the American Medical Association. The survey will permit classification of physicians according to qualifications as regards professional specialties, previous military experience, physical condition, and adaptability of the individual physician to the care of the civilian population or to the care of military personnel.

The State Committee on Medical Preparedness has requested each county medical society to appoint a parallel committee to supervise activities within its jurisdiction.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Society News.—Dr. Thomas C. Naugle, Gadsden, addressed the Etowah County Medical Society in Gadsden, June 18, on "Use of Sulfanilamide Compounds in Eye, Ear, Nose and Throat Treatment."—Dr. Seale Harris Jr., Birmingham, discussed "Practical Application of Some of the Newer Endocrine Products" before the Walker County Medical Society, June 14, in Jasper.

CALIFORNIA

Press Department to Be Established.—Resolutions were adopted by the council of the Los Angeles County Medical Association, June 3, which express the society's policy concerning public health education and approve the establishment of a department of press information, patterned after one operated by the New York Academy of Medicine. It will consist of a rotating voluntary committee of members of the association, selected for their qualifications in the various branches of medicine, sponsored by the sections and acting with the committee on public policy and relations together with the association officers. The group will give interviews to the press representatives by telephone or in person on pertinent medical matters, the names of the doctors to be used but not addresses or specialty, each to be a spokesman for the department and so announced in each press item. Each article published in the newspapers will bear the caption "This article is released in the interest of public health education and is approved by the Los Angeles County Medical Association."

COLORADO

Society News.—Dr. Constantine F. Kemper, Denver, addressed the Northeast Colorado Medical Society in Sterling, June 13, on pernicious anemia and recent advances in the treatment of ductless gland disorders.—Dr. Gerrit Heusinkveld, Denver, discussed "Subinvolution of the Uterus" before the San Luis Valley Medical Society in Monte Vista, June 18, and Dr. William H. Halley, Denver, policies of the state medical society.

Radiologic Conference.—The sixth midsummer radiologic conference, sponsored by the Denver Radiological Club, will be held at the Hotel Shirley-Savoy, Denver, August 8-10. Guest speakers include:

Dr. Howard B. Hunt, Omaha, Roentgenologic Aspects of Traumatic Disease in the Nervous System.
Dr. Fred E. Angle, Kansas City, Kan., Clinical Features of Brucellosis.
Dr. Howard P. Doub, Detroit, Tumors of the Small Bowel.

Dr. Albert Soiland, Los Angeles, Medical Aspects of Ultra Short Wave X-Rays.

Dr. Edwin C. Ernst, St. Louis, Mandibular Joint Syndrome.

Dr. Charles L. Martin, Dallas, Diagnosis and Treatment of Carcinoma of the Pharynx and Its Complications.

Dr. Lewis G. Allen, Kansas City, Kan., Radiation Therapy in Surgical Mumps.

A meeting Thursday evening will be a joint one with the Medical Society of the City and County of Denver with the following speakers:

Dr. Soiland, Value of the Radiologist to a Medical Community.

Dr. Ernst, Diseases and Their Roentgen Management.

Dr. Martin, Recent Advances in Radiation Treatment of Cancer.

Dr. Doub, Relationship of Industrial Trauma to the Formation of Hypertrophic Arthritis.

CONNECTICUT

Physician Honored.—Dr. James D. Gold, Bridgeport, president-elect of the Connecticut State Medical Society, was honored at a dinner given by present and former members of the council of the society to mark his retirement as chairman. Dr. Joseph I. Linde, New Haven, president of the society, presided. Dr. Gold was presented with an engraved pen and pencil.

DISTRICT OF COLUMBIA

Personal.—Drs. William Thornwall Davis and Tomas Cajigas, Washington, were decorated with the Order of Carlos J. Finlay recently at a reception at the Cuban Embassy. The presentation was made by Dr. Juan M. Moya, secretary of sanitation of Cuba.—Dr. Winfred Overholser, superintendent, St. Elizabeths Hospital, Washington, was awarded the honorary degree of doctor of science by Boston University, June 10.

Gift to Emergency Hospital.—The White Memorial Eye Operating Room, a gift from Mrs. Louise C. White in memory of her husband, George Whitney White, was recently dedicated at Emergency Hospital, Washington. The presentation was made by Dr. James N. Greear Jr., chief of the ophthalmic service at the hospital, on behalf of Mrs. White. Mr. White was a member of the board of directors of the hospital from 1910 until his death in 1938 and served as treasurer of the institution for seventeen years.

FLORIDA

State Board Officers.—Dr. Benjamin A. Chapman, Jacksonville, was elected president of the state board of medical examiners at a recent meeting in Tampa; Dr. Harold D. Van Schaick, Jacksonville, was named vice president, and Dr. William M. Rowlett, Tampa, was reelected secretary.

New Assistant State Health Director.—Dr. William H. Pickett, Clearwater, has been appointed assistant state health officer. The position was created on the recommendation of the American Public Health Association, following a survey of the health situation in Florida. Dr. Albert B. McCreary, Jacksonville, is state health officer. Dr. Pickett graduated at the Atlanta School of Medicine in 1911. His public health career includes two years spent as health officer of Pinellas County, two as health officer in Escambia County and eleven years as health officer first of Saginaw City and later of Saginaw County, Mich.

GEORGIA

Dr. Calhoun Honored.—The Fulton County Medical Society gave a dinner in honor of Dr. F. Plinizz Calhoun, Atlanta, at the Piedmont Driving Club, July 12, to mark his recent election as president of the American Ophthalmological Society. Dr. Calhoun graduated at Atlanta College of Physicians and Surgeons in 1904 and was professor of ophthalmology at Emory from 1912 to 1937.

Changes in Health Personnel.—Dr. Guy V. Rice Jr., Jesup, has resigned as health commissioner of Wayne County, effective June 15, to become medical director of the southwestern health region, with headquarters in Albany. He succeeds Dr. Lester M. Petrie, who has been transferred to the northeastern health region, Gainesville. Dr. Edward S. Armstrong, Cordele, resigned as commissioner of health in Crisp County, effective June 15, to become venereal disease control officer with the Savannah-Chatham County health department. Dr. Charles R. Smith, Morgan, has resigned as health commissioner of Calhoun County, effective July 1, to accept a similar position in Terrell County, succeeding Dr. Oliver W. Jenkins, Dawson.

ILLINOIS

Society News.—Dr. I. Pat Bronstein, Chicago, discussed "Endocrine Disturbances in Childhood" before the Madison County Medical Society in Madison, June 7.—Dr. Adrien H. Verbrugghen, Chicago, lectured on "Intractable Pain and Its Management" before the Kane County Medical Society in Geneva, June 12.—Dr. Melvin R. Guttman, Chicago, addressed the McHenry County Medical Society, July 25, on "Diagnosis and Treatment of Middle Ear Complications."—Dr. Charles F. Read, Elgin, was elected president of the Illinois Psychiatric Society at its annual meeting recently; Dr. Clarence A. Neymann, Chicago, was named vice president and Dr. Eugene I. Falstein, Chicago, secretary-treasurer.

Chicago

Course on Pediatrics.—The Children's Memorial Hospital will conduct a four weeks' graduate course in pediatrics, beginning September 30. The fee for the four weeks' course is \$100. Registration should be made at least one month before entrance if possible and should be accompanied by a \$10 deposit. This will apply on the fee for the course and will be refunded if the applicant is unable to participate. Inquiries should be addressed to Graduate Course, 707 Fullerton Avenue.

INDIANA

Pediatricians Elect Officers.—Dr. Kenneth T. Knode, South Bend, was elected president of the Indiana State Pediatric Society recently; Dr. John C. Burkle, Lafayette, vice president, and Dr. Matthew Winters, Indianapolis, secretary-treasurer.

Society News.—The Fountain and Warren Counties Medical Society was addressed at Covington, June 7, by Drs. Frank M. Gastineau and Norman M. Beatty, Indianapolis, on pathology and treatment of eczema.—A symposium on "lessons learned during seven years with a tumor group" was presented before the LaPorte County Medical Society, June 20, by Drs. Harry E. Mock, Charles E. Shannon and John L. Lindquist, all of Chicago.—Dr. Robert L. Glass, Indianapolis, addressed the Tippecanoe County Medical Society, Lafayette, June 25, on "Herniation of the Intervertebral Disk."—Dr. Robert M. Moore, Indianapolis, was the guest speaker before the Gibson County Medical Society, Princeton, June 10, on "The Heart at Middle Age."—Dr. John S. Robison addressed the Randolph County Medical Society, Winchester, June 26, on "Fracture of the Neck of the Femur."

IOWA

Personal.—Dr. Francis A. Ely, Des Moines, has been made an honorary alumnus of Jefferson Medical College of Philadelphia. The honor was conferred to mark the gratitude of the university and its alumni to Dr. Ely's grandfather, the Rev. Ezra Stiles Ely, who, while serving as pastor of the Old Pine Street Presbyterian Church and as secretary of the additional board of trustees of the college, came to the rescue of the school when it was in financial difficulty.—Dr. Lindsey J. Ervin, director of the venereal disease service at Broadlawn General Hospital, Des Moines, has been named temporary director of the Polk County health unit. He succeeds Dr. Edwin N. Hesbacher, who recently was appointed to the staff of the U. S. Marine Hospital in Detroit. Dr. Hesbacher served as director of the health unit for a year.

KENTUCKY

Changes in Health Officers.—Dr. Aubrey Y. Covington, Morganfield, has resigned as health officer of Union County to take a similar post in Scott County, with headquarters in Georgetown. Dr. Covington succeeds Dr. Carl M. Gambill, who has joined the staff of the state health department.—Dr. Donald B. Thurber, Louisville, has been appointed health officer of Nicholas County, with headquarters at Carlisle, succeeding Dr. James W. Scudder, who has been appointed to the staff of the Western State Hospital, Hopkinsville.—Dr. George B. Davis, Glasgow, recently health officer of Barren County, has been appointed to a similar position in Hart County.

Society News.—Dr. Irving J. Wolman, Philadelphia, addressed the Jefferson County Medical Society, Louisville, June 17, on "Advantages of Milk in the Diet."—At a meeting of the Warren-Edmondson County Medical Society in Bowling Green, May 29, the speakers were Drs. Alexander M. Forrester Jr., Louisville, on "Modern Treatment of Middle Ear

Disease"; Charles F. Wood, Louisville, "Injuries to the Knee Joint," and David Woolfolk Barrow, Lexington, "Treatment of Thrombophlebitis and Vascular Diseases of the Extremities."—Speakers at a meeting of the Harlan County Medical Society, Harlan, June 29, were Drs. Arthur T. McCormack, secretary of the Kentucky State Medical Association, on the service of physicians in national defense; Philip F. Barbour, heart disease in children, and Lytle Atherton, diseases of the kidney. All are of Louisville.

MAINE

State Medical Meeting and Election.—At the eighty-eighth annual session of the Maine Medical Association in Rangeley Lakes, June 23-25, Dr. Penry L. B. Ebbett, Houlton, was chosen president-elect and Dr. Thomas A. Foster, Portland, became president. Dr. Frederick R. Carter, Augusta, is the secretary. Included among the out of state speakers were the following:

- Dr. David G. Cogan, Cambridge, Mass., Some Oculomotor Disturbances.
- Dr. Trygve Gundersen, Boston, Diagnosis and Treatment of Some Corneal Conditions.
- Dr. Ralph M. Tovell, Hartford, Conn., Pentothal Sodium: Its Field of Usefulness.
- Dr. Meyer Saklad, Providence, R. I., Anesthesia and Disturbed Physiology.
- Dr. Sven M. Gundersen, Hanover, N. H., Diabetes: The Problem from the Standpoint of the Internist.
- V. W. Peterson, special agent in charge, Federal Bureau of Investigation, Boston, Modern Criminal Detection.
- Dr. Moses Ralph Kaufman, Boston, Psychotherapy in General Medical Practice.
- Dr. Henry C. Marble, Boston, Compound Injuries to the Hand.
- Dr. Timothy Leary, Boston, Traumatic Intracranial Hemorrhages with Demonstration of Brains.

A clinicopathologic conference was conducted with Dr. Reginald Flitz, Portland, in charge. At the annual dinner, the speakers were P. S. Demers, Springvale, representing the Maine Pharmaceutical Association, and Gov. Lewis O. Barrows. Fifty year gold service medals were presented to Drs. Henry H. Brock, Portland, and Frederick B. Adams, now of Tampa, Fla. Dr. Leary and Franz U. Burkett, attorney general, Portland, were special guests of the Maine Medico-Legal Society in joint session with the medical examiners of the state.

MICHIGAN

"Cancer Specialist" Under Surveillance.—Edward La Motte, Garden, who represented himself as a "cancer specialist," pleaded guilty recently to a charge of practicing medicine without a license, according to the state medical journal. La Motte has been placed on probation for three years, during which time he must make monthly appearances before the judge who sentenced him to prove he is not practicing medicine in any form in Michigan, under penalty of spending six or more months in jail, it was stated.

Physicians Honored.—A public banquet was held in Northport, June 26, to honor Dr. Robert E. Flood on his seventieth birthday and completion of forty years of practice in the community. Nearly 200 persons attended the banquet, at which Dr. Burton R. Corbus, Grand Rapids, president of the Michigan State Medical Society, made the principal address. Dr. Flood received a testimonial plaque commemorating the occasion.—The Alpena-Presque Isle-Alcona Counties Medical Society gave a banquet, June 5, in honor of Dr. Clarence A. Carpenter as a tribute to his years of service in Onaway. He received several gifts. Dr. Carpenter has been practicing medicine for forty-two years. He has served as health officer in Onaway and was the first president of the Presque Isle County Medical Society before it became part of the tri-county organization.—Dr. Frank H. Bethell, Ann Arbor, was given one of the two annual Henry Russel awards at the University of Michigan, Ann Arbor, for his "direction of field studies of anemias of pregnancy in Hillsdale County" in cooperation with the W. K. Kellogg Foundation, newspapers recently reported. The awards are given to the young faculty members who show promise.

MINNESOTA

Illegal Practitioner Jailed.—John Taylor, alias "Hobo Jack," pleaded guilty in the district court of Benton County, June 12, to a charge of practicing healing without a basic science certificate. He was sentenced to pay a fine of \$100 plus court costs of \$23.15 or to serve ninety days in the county jail of Stearns County, Benton County having no county

jail. Taylor was unable to pay the fine and the court remanded him to the custody of the sheriff to serve his sentence. Taylor was arrested June 7, and it was proved that he had been diagnosing the ailments of farm people and prescribing various medicines, the state board of medical examiners reported. He represented himself as "Hobo Jack," the unlicensed specialist, and claimed to be able to cure arthritis, disease of the prostate, hemorrhoids, stomach ulcers and many other ailments. Taylor admitted that he never studied medicine but that he had practiced unlawfully in California, Oregon and Washington. He said that he had never previously been arrested.

MISSISSIPPI

Society News.—The Northeast Mississippi Thirteen Counties Medical Society was addressed in Macon, June 11, by Drs. Otis B. Crocker, Bruce, "Practical Points in the Differential Diagnosis and Treatment of Appendicitis"; John C. Culley, Oxford, and Thomas H. Blake, Jackson.

Public Health Personnel.—Dr. Taswell Paul Haney Jr., who has been on leave of absence the past year from his position as director of the Pike County health department, McComb, has been appointed director of maternal hygiene and child welfare of the Mississippi State Board of Health. Dr. George E. Riley, Jackson, director of malaria control work in the state health department, has been named in charge of Pike County, and Dr. David B. Wilson, McComb, who has been acting director of the county unit, has accepted a position with the U. S. Public Health Service.

MISSOURI

The Robert James Terry Lecture.—The late Dr. William T. Coughlin, professor of surgery, St. Louis University School of Medicine, St. Louis, bequeathed \$5,000 in his will to the St. Louis Medical Society to establish and maintain an annual lecture to be known as the "Robert James Terry Lecture."

New Director of Health of Kansas City.—Dr. Hugh L. Dwyer has been appointed director of health of Kansas City to succeed Dr. Edwin L. Schorer. Dr. Dwyer is professor of clinical pediatrics at the University of Kansas School of Medicine, Kansas City-Lawrence. He graduated at Tulane University School of Medicine, New Orleans, in 1918.

MONTANA

Sale of Drugs Restricted.—The Montana State Board of Pharmacy has announced that, effective July 1, certain drugs must be sold only on the prescription of regularly licensed physicians, dentists or veterinarians, newspapers reported June 29. Included in the list of drugs which are designated as "dangerous, hypnotic or habit forming" are aminopyrine, barbituric acid, amphetamine, cinchophen, sulfanilamide and sulapyridine. The action of the state board of pharmacy was taken at the request of the state board of health and the Montana State Medical Association.

NEW JERSEY

Personal.—A portrait of Dr. Edward J. Ill, Newark, was unveiled at a dinner recently as an event of the seventy-fifth anniversary celebration of the Hospital of St. Barnabas for Women and Children, Newark. It will be hung in the hospital in recognition of Dr. Ill's fifty-eight years of service on the staff. Dr. Ill is 86 years old and is still practicing.

NEW YORK

Trichinosis Traced to Sausage.—Investigation of an outbreak of thirty-five cases of trichinosis in New York, New Rochelle and Mount Vernon showed that all the victims had eaten sausage called "teewurst," made of raw pork smoked at 85 F., for twenty-four hours. It appeared that all the sausage came from one dealer and the dates of purchase indicated that it was all from the same batch.

Annual Meeting at Lake Keuka.—The forty-first annual meeting of the Lake Keuka Medical and Surgical Association was held at Penn Yan, June 20-21. On the scientific program were the following speakers:

- Dr. Theodore C. Erickson, Montreal, Management of Head Injuries.
- Dr. Gershom J. Thompson, Rochester, Minn., Transurethral Prostatectomy.
- Dr. Robert B. McGraw, New York, Shall We Have Fewer or More Psychiatrists?

Dr. Samuel H. Geist, New York, Practical Gynecologic Endocrinology.
Dr. Neil W. Swinton, Boston, Diagnosis and Management of Precancerous Lesions of the Rectum and Colon.

Dr. Arthur W. Booth, Elmira, chairman of the Board of Trustees, American Medical Association, and Dr. Terry M. Townsend, New York, immediate past president of the Medical Society of the State of New York, opened the program with addresses.

New York City

Salmon Memorial Lectures Changed.—Because of the uncertainties of international transportation, Dr. Alexander Luria, Moscow, Russia, will not give the Salmon Memorial Lectures for 1940 and Dr. Nolan D. C. Lewis, director of the New York State Psychiatric Institute, has been appointed lecturer in his stead. The dates of the lectures have also been changed to November 8, 15 and 22. They will be delivered at the New York Academy of Medicine.

Health Center Areas Established.—The city planning commission has established thirty health center districts as locations for health centers, in accordance with a plan submitted by Dr. John L. Rice, city health commissioner, in May 1939. Dr. Rice's program called for construction of fourteen district health centers and twenty-three subcenters between 1940 and 1945 at an estimated cost of \$7,550,000. When the report was submitted, nine new health centers were in operation, five were under construction and about \$4,500,000 had been expended since 1934 on such projects.

Gifts to New York University.—Gifts including \$28,247 for medical research were recently announced by New York University. Among them were:

John and Mary R. Markle Foundation, \$2,850 for research under Dr. Norman H. Jolliffe, associate professor of medicine.

Metropolitan Life Insurance Company, \$1,735, and two anonymous donors, \$1,100 for research on pneumonia under Dr. Jesse G. M. Bullowa.

National Committee on Maternal Health, \$1,870 for the Robert L. Dickinson research fellowship fund at the Washington Square College; \$300 for the department of neurology, college of medicine.

Lederle Laboratories, \$1,000 on a \$4,000 grant for research on digitalis glucosides under Dr. Arthur C. DeGraff; \$625 for the Lederle Fund.

Estate of James W. Keenan, \$1,366.69 to establish a memorial fund for surgical research.

Commonwealth Fund, \$4,266.65 on a grant to the department of preventive medicine; \$3,798.75 for research in obstetrics and gynecology under Dr. William E. Studdiford Jr., and \$2,150 for study of hypertensive and renal diseases under Homer W. Smith, Sc.D., department of physiology.

Rockefeller Foundation, \$1,250 for research in cellular physiology under Robert Chambers, Ph.D., department of biology, Washington Square College.

International Cancer Research Foundation, \$1,000 for research on cancer under Professor Chambers.

New York Foundation, \$1,000 for the New York Foundation for Experimental Surgery under Dr. Benjamin G. P. Shafiroff, instructor in surgery, college of medicine.

Anonymous donor, \$1,000 for research in therapeutics, college of medicine.

NORTH CAROLINA

Society News.—Dr. Otto Billig, Asheville, addressed the Buncombe County Medical Society, Asheville, June 17, on "Insulin Shock and Subshock Treatment in Mental Disease." —Dr. John Herman Long, Baltimore, addressed the Guilford County Medical Society, Greensboro, June 6, on "Chemotherapy in Gynecology" and "Endocrine Therapy in Gynecology."

Public Health Meeting.—Dr. John W. Williams, Williamston, was elected president of the North Carolina Public Health Association at the recent annual meeting in Pinelhurst; Dr. Robert E. Rhyne, Gastonia, vice president, and Dr. John S. Anderson, Raleigh, secretary. Among the speakers were Drs. John A. Ferrell and Daniel F. Milam of the International Health Board of the Rockefeller Foundation; Joseph C. Knox, state epidemiologist, and Franklin C. Smith, Charlotte, who discussed vision testing in school children.

Symposiums on Obstetrics and Pediatrics.—A symposium on obstetrics and pediatrics was held at Roaring Gap, June 16-17, under the auspices of the state board of health and the postgraduate committee of the Medical Society of the State of North Carolina. Dr. Julius H. Hess, Chicago, discussed "Prematurity" and "Bronchiectasis in Childhood," and other speakers included Drs. Williamson Z. Bradford, Charlotte, "Toxemia of Pregnancy"; Thomas Leslie Lee, Kinston, "Placenta Praevia," and Francis Bayard Carter, Durham, "Ablatio Placentae." —A similar symposium was held at Wrightsville Beach, June 23, with the following speakers, among others: Drs. Edward A. Schumann, Philadelphia, on

"Complications of Pregnancy Other Than Hemorrhage" and "Hemorrhage in Pregnancy and Labor"; Charles P. Mangum, Richmond, Va., "Pediatric Endocrinology"; Jay M. Arena, Durham, "Congenital Syphilis," and James Buren Sidbury, Wilmington, "Treatment of Diarrhea and Intestinal Intoxication."

OHIO

District Meeting.—The annual meeting of the eighth district of the Ohio State Medical Association was held at Rocky Glen Sanatorium, McConnellsville, June 20. The speakers on the scientific program were Drs. Chevalier L. Jackson, Philadelphia, on "Bronchoscopy and Bronchography as Aids in the Diagnosis and Treatment of Bronchopulmonary Diseases" and Andre Crotti, Columbus, "Some of the Latest Conceptions of the Cause of Cancer."

Personal.—Dr. George W. Crile, Cleveland, has been made an honorary member of the Academy of Medicine of Cleveland. —Dr. Reaves W. DeCrow, Columbus, has been appointed health officer of Clinton County. —Dr. George E. French has retired after thirty-seven years as health officer of Elyria, it is reported. Dr. Harold A. Robinson, Elyria, is his successor. —Dr. Abraham Strauss has been appointed chief of the surgical department of Mount Sinai Hospital, Cleveland, succeeding the late Dr. Moses E. Bland. —Dr. Millard C. Hanson, health director of Toledo since April 1937, has resigned to become director of a syphilis control program in Pittsburgh.

Dr. Gebhard to Direct Health Museum.—Dr. Bruno Gebhard, former curator of the Hygiene Museum in Dresden, Germany, has been appointed director of the Cleveland Museum of Health and Hygiene, which is to open in October. Dr. Gebhard left Germany in 1937 and has been serving as technical consultant for the medicine and public health exhibits at the World's Fair in New York. Plans for the museum were launched in 1939 when Mrs. Francis F. Prentiss donated a building for the purpose and the Cleveland Academy of Medicine carried out a campaign for supporting memberships. In addition to exhibits for education in public health, the museum expects to have workshops for the creation of visual health aids for schools, colleges and other educational agencies.

OKLAHOMA

Care of Crippled Children.—Aided by a grant from the Children's Bureau, the Oklahoma Commission for Crippled Children has established a rheumatic fever and heart service. The work is carried out through the department of pediatrics of the University of Oklahoma School of Medicine and the Crippled Children's Hospital, Oklahoma City. Clinics are held and eight beds have been set aside in hospitals for patients with active infection. A new ward of sixteen beds has been opened in the Crippled Children's Hospital for Negro children.

OREGON

Personal.—Dr. Adolph Weinzirl, Portland, was elected president of the Oregon Health Officers' Association at the recent annual meeting in Astoria. Dr. Abraham A. Merkel, Medford, is vice president and Dr. A. Edward Bostrom, Portland, secretary. —Dr. Wilbur M. Bolton, Portland, was elected president of the Alumni Association of the University of Oregon Medical School at the recent annual meeting. Dr. Edmund H. Berger, Portland, was elected secretary. —Dr. Harold M. Erickson, The Dalles, has been appointed director of the division of maternal and child health in the state board of health to succeed Dr. George D. Carlyle Thompson, Portland, who resigned to take a position with the U. S. Children's Bureau.

PENNSYLVANIA

District Meeting.—The Sixth Councilor District of the Medical Society of the State of Pennsylvania met in Birmingham, July 11. On the scientific program were Drs. Joseph D. Findley, Altoona, speaking on "The Present Status of Industrial Medicine," and Howard A. Power, Pittsburgh, "Prophylactic Management of Obstetric Difficulties." Drs. Charles H. Henninger, Pittsburgh, president of the state society; Walter F. Donaldson, Pittsburgh, secretary, and Chauncey L. Palmer, Pittsburgh, chairman of the committee on public health legislation, and John J. Shaw, state secretary of health, Harrisburg, made addresses, and fifty year testimonial certificates were presented to Drs. William H. Banks, Mifflintown, Charles M. Johnson, McVeytown, Brooklyn E. Levengood, Bellwood, and Henry W. Sweigart, Lewistown.

Philadelphia

Alumni Reunion Plans.—The 1911 class of the University of Pennsylvania School of Medicine will hold its thirtieth reunion, Thursday, September 19, at Pine Valley Country Club, Clementon, N. J. Information about accommodations may be obtained from Dr. John P. Chapman; information about the university's bicentennial program from Dr. Thomas Grier Miller. Class dues of \$10 may be sent to Dr. Wilbur H. Haines, secretary, 255 South Seventeenth Street.

Osler Memorial Dedicated.—The old autopsy house at the Philadelphia General Hospital, where Dr. William Osler worked from 1885 to 1889, has been restored to be used as a museum of Osleriana and was dedicated in June. Eleven resident physicians who served with and under Dr. Osler were present, as was Dr. Howard A. Kelly, Baltimore, the only living member of the famous group who served with Osler at Johns Hopkins. Dr. Joseph McFarland, who was resident physician at the hospital, then known as Blockley, in 1889, spoke on "Osler as I Knew Him," and Dr. William G. MacCallum, Baxley professor of pathology, Johns Hopkins University School of Medicine, Baltimore, a former pupil, spoke on "Osler at Blockley." Other speakers were Dr. William E. Hughes, physician at the hospital from 1889 to 1914 and now honorary consultant, and Dr. William E. Robertson, who paid tribute to Dr. David Riesman, one of those most active in the establishment of the memorial. Dr. Riesman died a week before the dedication. An important feature of the ceremonies was the unveiling of a painting by Dean Cornwell, "Osler at Old Blockley," for John Wyeth & Brother, Inc., who also financed the restoration of the building.

RHODE ISLAND

Society News.—The Providence Medical Association was addressed, June 3, by Drs. Roland Hammond on "The Oldest Scientific Book in the World—The Edwin Smith Surgical Papyrus," and Ira C. Nichols, "Delirium as a Danger Signal."—At the annual spring clinic of the Providence Hospital Intern Alumni Association the guest speakers were Drs. Paul L. Cusick, Rochester, Minn., on "Ophthalmic Examinations from the Viewpoint of the General Practitioner" and Harry L. Alexander, St. Louis, "Physical Examination of the Patient, Stressing Emphysema."

TEXAS

District Meeting.—The Southwest Texas District Medical Society (Fifth and Sixth districts) held a meeting in McAllen, June 28-29, with the following speakers, among others:

- Dr. Walter G. Stuck, San Antonio, Fractures of the Hip.
- Dr. Edward W. Coyle, San Antonio, Collapse Therapy in the Treatment of Pulmonary Tuberculosis.
- Dr. Sidney W. Bohls, Austin, Some Problems in Virus Disease in Texas.
- Dr. George Van Amber Brown, McAllen, Drainage in Abdominal Surgery Based on Physiologic Principles.
- Dr. Hugh D. White, Monterrey, Mexico, Spinal Anesthesia.
- Dr. Ulysses S. Marshall, Weslaco, Symptoms and Physical Findings in Typhus Fever.

VIRGINIA

Special Society Meeting.—The Neuropsychiatric Society of Virginia held its spring meeting at St. Albans Sanatorium, Radford, June 19. Speakers included Drs. John C. Palmer of the sanatorium staff on "Experiences with Insulin and Metrazol in the Treatment of Eighty Psychotic Patients" and James N. Williams, Richmond, gave an interpretation of drawings made by maladjusted children.

WASHINGTON

Poliomyelitis in Pierce County.—The outbreak of poliomyelitis in Tacoma and Pierce County continues, but there are indications that it has passed its peak, according to *Northwest Medicine* for July. Eighty cases had occurred up to June 26. Nine patients had been treated in respirators and seven deaths had occurred. Less than one fourth of the patients suffered any paralysis, the report said. One case has been reported in King County and one in Kitsap County. Both of these had contacts in Pierce County. Sporadic cases have been reported from Snohomish County and the Grand Coulee district, it was said. Dr. Don W. Gudakunst, medical director of the National Foundation for Infantile Paralysis, is conducting an epidemiologic study.

WEST VIRGINIA

Society News.—Dr. James Edwin Wood Jr., Charlottesville, Va., addressed the Cabell County Medical Society, Huntington, June 13, on "Recent Experimental Studies in Hypertension and Their Relation to Practical Problems."—Dr. John W. Holloway, Cleveland, addressed the Kanawha County Medical Society, Charleston, June 4, on "Surgical Diseases in Children."—Dr. John M. Meredith, Charlottesville, Va., addressed the Logan County Medical Society, Logan, June 5, on "Treatment of Acute Head Injuries."—At a meeting of the Monongalia County Medical Society, Morgantown, June 4, the speaker was Dr. Delmas E. Greenelch, Wheeling, on spinal anesthesia.

WISCONSIN

Society News.—Drs. Robert von der Heydt and Oliver E. Van Aylae, Chicago, were guest speakers at a meeting of the Central Wisconsin Society of Ophthalmology and Otolaryngology at Land o' Lakes June 8-9.

Institutes on Diseases of the Chest.—A series of ten one day institutes on diseases of the chest will be presented during the weeks of August 5 and 12 under the sponsorship of the Wisconsin Anti-Tuberculosis Association, the committee on chest diseases of the State Medical Society of Wisconsin, the state board of health and Wisconsin sanatoriums. The institutes are financed by a fund left to the tuberculosis association by the late Dr. Hoyt E. Dearholt, Milwaukee, executive secretary for many years. The speakers who will take part are Drs. John A. Carswell, associate executive secretary of the tuberculosis association, and Arthur A. Pleyte, director of its medical department, Milwaukee; Herbert H. Christensen, Wausau; Harold M. Coon, Statesan; Frank L. Jennings, Indianapolis; John D. Steele Jr., Milwaukee, and Reuben H. Stiehm, Madison. The institutes will be held at sanatoriums in Winnebago, Plymouth, Whitelaw, West DePere, Wausau, Bayfield, Eau Claire, Onalaska, Janesville and Racine.

WYOMING

State Medical Meeting in Sheridan.—The annual meeting of the Wyoming State Medical Society will be held in Sheridan, August 11-13, under the presidency of Dr. John H. Goodnough, Rock Springs. Guest speakers will be:

- Dr. Arthur E. Hertzler, Halstead, Kan., Uterine Prolapse.
- Dr. Kenneth D. A. Allen, Denver, Practical Considerations of Certain Diseases of the Cervix Uteri with Relation to Prevention of Cancer.
- Dr. Frederick R. Harper, Denver, Some Practical Points in the Treatment of Empyema.
- Dr. Claude F. Dixon, Rochester, Minn., The General Practitioner's Role in Certain Intestinal Diseases.
- Dr. Kemp G. Cooper, Denver, Gastroscopy and Its Use in the Diagnosis of Stomach Pathology.
- Dr. Charles F. Moon, Omaha, Management of Labor in the Primipara.
- Dr. Peter T. Bohan, Kansas City, Mo., Arthritis: Special Reference to Etiology and Management.
- Dr. Charles Douglas Deeds, Denver, Recent Advances in the Treatment of Heart Disease.
- Dr. Ralph M. Stuck, Denver, A Review of the Surgical Treatment of Hypertension.

In addition, Wyoming speakers will be:

- Dr. Earl E. Whedon, Sheridan, Tonsillectomy Experiences in Private Practice.
- Dr. Robert I. Bump, Cheyenne, Cyclopropane as an Anesthetic Agent.
- Dr. Edward B. Speir, Cheyenne, Surgical Procedures in the Colon and Rectum.
- P. R. Carlquist, Cheyenne, The Services of the Public Health Laboratory.

HAWAII

Territorial Meeting and Election.—Dr. Paul Withington, Honolulu, was elected president of the Hawaii Territorial Medical Association at the recent annual meeting on Maui. Vice presidents were elected as follows: Drs. Gardner Black, Honolulu; Charles Bruce Brown, Hilo; Yen P. Chang, Lihue, and Ransom J. McArthur, Wailuku. Dr. Alfred L. Craig, Honolulu, was elected secretary. Dr. Isidor S. Ravdin, Philadelphia, was the guest speaker, discussing "Problems of Acute Appendicitis" and "Nutritional Problems in Surgical Patients."

PUERTO RICO

Society News.—Dr. Antonio Navas-Torres, San Juan, addressed the San Juan County Medical Society, June 28, on "Aniseikonia, a Great Promise in the Treatment of Asthenopia."—Dr. Jacobo Simonet, San Juan, was elected president of the General Antituberculosis Association of Puerto Rico at its annual meeting, June 30, and Dr. Oscar G. Costa-Mandry, San Juan, vice president.—Dr. George Draper, New York, addressed the Puerto Rico Medical Association recently on "The Man Within the Patient."

GENERAL

Interstate Malaria Survey.—States of the Upper Mississippi Basin are cooperating with the U. S. Public Health Service in an interstate malaria survey, which began the first week in July and will continue through the summer and fall. The work is administered by a board made up of the health commissioners of the states concerned, Minnesota, Wisconsin, Illinois, Missouri and Iowa, with Dr. Walter L. Bierring, Des Moines, Iowa, as chairman. Joseph A. LePrince, for many years sanitary engineer with the public health service, is directing the survey. Headquarters for the project are in the Federal Building, Rock Island, Ill.

Institute for Traffic Safety Training.—The third National Institute for Traffic Safety Training, sponsored by the National Safety Council and ten other interested organizations, will be held at the University of Tennessee, Knoxville, August 12-24. The institute provides short courses for advanced safety students, including the following topics, among others: advanced methods of adult driver training, traffic safety education in schools, traffic accident reports and records. There will also be general meetings to discuss the standard highway safety program. Information may be obtained from Mr. Sidney J. Williams, 20 North Wacker Drive, Chicago.

National Medical Association.—The forty-sixth annual meeting of the National Medical Association will be held in Houston, Texas, August 12-16, jointly with the National Hospital Association and the National Insurance Medical Examiners Association. There will be several joint sessions with panel discussions and addresses by representatives of the American Medical Association, the Texas State Medical Association and the National Bar Association. Medical, surgical and pharmaceutical sections will meet Tuesday, Thursday and Friday. Dr. Albert W. Dumas Sr., Natchez, Miss., is president of the association and Dr. John T. Givens, Norfolk, Va., is secretary.

Advisory Board for Palestine Medical Program.—Hadassah, the women's Zionist organization in the United States which has sponsored the building of the Rothschild-Hadassah-University Hospital and Medical School in Palestine, recently announced a medical advisory board to advise the organization on professional problems arising from the hospital, child welfare and public health activities. Dr. Ephraim M. Bluestone, New York, is chairman of the board, which includes also Drs. Jacob J. Golub, Sigismund S. Goldwater, Emanuel Libman and Nathan O. Ratnof, Maurice B. Hexter, Ph.D., all of New York; Dr. Jonas S. Friedenwald, Baltimore; Louis I. Dublin, Ph.D., New York, and Abel Wolman, D.E., Baltimore.

Fellowships in Chemistry.—For the academic year 1940-1941 Abbott Laboratories has established fellowships in several universities with important departments of organic chemistry and biochemistry. The fellowships, carrying stipends of \$650 a year, will be available to graduate students in the last or next to last year of graduate work leading to the doctorate degree. The recipients, who are to be selected by the universities in which their work is being done, are not limited as to the subjects on which they will work. The object of the fellowships is to provide means for the carrying on of additional scientific work in American universities. Grants for work in organic chemistry will be made to Cornell, Harvard, Illinois and Michigan universities and in biochemistry to California, Columbia and Cornell.

Cancer Society Offers Prizes for Poster.—A nationwide competition for posters designed to stimulate public interest in the control of cancer has been announced by the American Society for the Control of Cancer. Prizes amounting to \$1,875 will be awarded by a jury of artists, publicists and scientists. The National Alliance of Art and Industry will receive the posters from October 1 to 12, the awards will be made October 14 and the best posters will be exhibited for two weeks beginning October 16 in the National Arts Club, 15 Gramercy Park. The competition is open to all artists and art students. A contestant may submit as many designs as he wishes. Artists who wish additional information about cancer or the work of the American Society for the Control of Cancer may obtain literature from the society at 350 Madison Avenue. Details about the competition may be obtained from the National Alliance of Art and Industry, 119 East Nineteenth Street, New York.

Board Examinations in Ophthalmology.—The American Board of Ophthalmology announces that the only written examination in 1941 will be held in various cities March 8. Candidates enrolled in the preparatory group who have been advised that they will be eligible for examination during 1941

should make application at once to take this written examination. Applications must be made on the regular blanks provided for the purpose and must be received in the office of the board before December 1. Oral examinations will be held in Cleveland in May or June 1941, and in October at another place to be announced later. The deadline for case reports for the Cleveland examination is Feb. 1, 1941, and for the October examination, July 1, 1941. A special oral and clinical examination will be held on the Pacific Coast during 1941 provided there are enough candidates to warrant it. Applications for this examination should be filed before September 1940 so that the board may complete necessary arrangements.

Society News.—New officers of the American Laryngological Association elected in May include Drs. Gordon Berry, Worcester, Mass., president; Charles T. Porter, Boston, and Gordon F. Harkness, Davenport, Iowa, vice presidents.—Dr. Jack C. Norris, Atlanta, Ga., was elected president of the American Association of Medical Milk Commissions at the annual meeting held jointly with the Certified Milk Producers' Association in New York in June. Dr. Paul B. Cassidy, Philadelphia, was elected secretary of the association of milk commissions.—Dr. Henry J. Walton, Baltimore, was elected president of the American College of Radiology at its annual meeting in New York, June 12, and Dr. Sherwood Moore, St. Louis, vice president; Dr. Hollis E. Potter, Chicago, was reelected treasurer, and Mr. Mac F. Cahal, Chicago, was reelected executive secretary. The next annual meeting of the college will be held in Cleveland on Wednesday during the week of the annual session of the American Medical Association.

Provisional Mortality Rates for 1939.—The Bureau of the Census announces that provisional tabulations of deaths in continental United States in 1939 show a crude death rate of 10.7, as compared with 10.6 for 1938. The bureau points out that the apparent increase may be due to the use of the 1938 estimate of population in computing the 1939 rate and that the difference may disappear or be reversed when the new census figures are available. Rates for individual states are computed on 1937 estimates of population and are therefore higher for some states than they would be if computed on 1939 estimates. Twenty states show lower crude rates in 1939 than in 1938, twenty-one states and the District of Columbia show higher rates and seven states show no change, the report said. The greatest decreases occurred in Rhode Island, South Carolina, Georgia, North Carolina, Alabama and Arizona; the largest increases in the District of Columbia, Idaho, Iowa and Montana. The highest rates were for Arizona (14.2 per thousand of population), New Mexico (14.1), District of Columbia (13.2) and Florida (12.8). The lowest rates were for North Dakota (7.7), Oklahoma and South Dakota (8) and Arkansas (8.1). The report emphasized that differences in crude death rates do not necessarily indicate corresponding differences in health conditions. Age, sex and racial distributions are factors that affect the crude death rate, and these distributions differ in the various states.

FOREIGN

Personal.—The Osler Memorial Medal of the University of Oxford, England, was recently awarded to Sir E. Farquhar Buzzard, regius professor of medicine in the university.—The Académie de médecine, Paris, has awarded the Helme Prize to Dr. André Gratia, professor of bacteriology, Liège University, for his work on bacteriophages.

Prize for Encephalitis Research.—The University of Berne, Switzerland, recently announced its annual prize for work on encephalitis lethargica which "signifies real progress in the diagnosis or treatment of the disease." Those who wish to participate should send their applications to the dean of the Medical Faculty of Berne, which allocates the prize at the end of each year.

Sir James Barrett Honored.—A portrait of Sir James Barrett, who was associated with the University of Melbourne, Australia, for more than forty years until his retirement in 1939, was recently presented to him by the university council and staff, medical graduates and other citizens. Sir James, who presented the portrait to the university, began his career with the university as demonstrator in physiology and later was appointed lecturer in the physiology of the special senses, an office which he held for some forty years. In 1901 he became a member of the university council, in 1931 vice chancellor and in 1935 chancellor. Sir James has served not only the medical school and the university, but the city of Melbourne in widely diverse fields. He has been active in the development of musical affairs and is known as a naturalist.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 3, 1940.

A New Industry—Growing Vegetable Drugs

Because of the use of shipping for the importation of munitions, space for the carriage of the large amount of food imported is restricted and therefore more food is being grown at home. Similarly the scarcity of certain imported drugs from the cutting off of supplies from enemy or occupied countries has led to a movement for the growing of drugs which previously were imported. Operators on the New York drug market are scouring the world for new sources of vegetable drugs, and the same can be said of the London drug market. With supplies cut off from a large portion of central Europe, the Netherlands, Belgium and Italy and with shipments from France and Mediterranean countries disorganized, most of the world's production of vegetable drugs is denied to the majority of consumers. It is curious that America, with its variety of soils and climates, pays tribute to foreign nations for the bulk of the raw materials for the remedies its population consumes so abundantly. It is also remarkable that few varieties of vegetable drugs are cultivated on a large scale in the British Empire and that production in the British Isles is trivial. It has therefore been suggested that, just as amateur gardeners are now adding substantially to the country's supply of food, so it should be possible for them to market considerable quantities of the many vegetable drugs which grow well in the soils of Great Britain and Ireland. Plans have already been made for more intensive cultivation on medicinal plant farms which exist in England. The pharmaceutical, Linnean (botanic) and chemical societies are taking an interest in the project.

The Canadian Red Cross Hospital

The Canadian Red Cross Hospital for sick and wounded Canadians occupies 22 acres on Viscount Astor's estate near Taplow. This ground was occupied by a Canadian hut hospital in the last war and has been leased to the Canadian Red Cross by Lord Astor at a rent of a quarter of a dollar a year. The cost of erecting and equipping the hospital (the equipment is still incomplete) is about \$1,000,000. There are fifteen wards, each accommodating thirty-six or, in an emergency, fifty beds, which are reached by a long corridor running the whole length of the building. There is a special wing for officers and a complete operating block and x-ray department. The furniture is of Canadian maple in early colonial design. Each ward opens on a sun porch. There are four operating rooms and special clinics for dental, eye, ear and nose cases. A special laboratory is being furnished to the requirements of Sir Frederick Banting, the eminent Canadian who is director of the pathologic department. The officers connected with the hospital include Col. George G. Nasmith, former health officer in Canada, who was attached to the mobile field laboratory of the British Expeditionary Force in 1915 and is now deputy commissioner of the Canadian Red Cross Society in London; Major C. A. Scott, Assistant Commissioner; Col. R. M. Luton, senior medical officer with the Canadian Forces; Major J. C. McKenzie, general superintendent of the Montreal General Hospital, and Col. C. L. T. Arthur, a well known Winnipeg physician, who is in charge of the staffing of the hospital. The matron-in-chief of the Canadian Military Nursing Services is Miss E. F. Pense, who served as a nurse with the Canadians in the last war.

Sir Arthur Harden

Sir Arthur Harden, F.R.S., late head of the Biochemical Department of the Lister Institute and emeritus professor of biochemistry, London University, has died at the age of 75.

In 1929 the Nobel prize for chemistry was divided between him and Professor von Euler of Stockholm. In 1935 he was awarded the Davy medal of the Royal Society for his work in biochemistry and especially for his discoveries in fermentation. In 1906 he discovered that the fermentation of sugar depended on a specific activator which was not an enzyme and which was essential for the process. He also discovered that phosphates were an equally necessary factor. From 1913 to 1937 he was joint editor of the *Biochemical Journal*.

BUENOS AIRES

(From Our Regular Correspondent)

June 24, 1940.

Diphtheria Carriers

The National Council of Education ruled in 1933 that children attending schools, who have reported sick with diphtheria, shall be examined as to the presence of Loeffler's bacilli in the throat every eight days until two consecutive negative results have been obtained. Since 1937 these bacteriologic examinations have consisted in cultures in Horgan and Marshall's medium with 0.16 per cent tellurite, observed twenty-four hours after inoculation. Dr. Rietti has reported to the Argentine Society of Biology the results of 11,921 cultures made in 5,840 cases; 877, 15 per cent, showed bacilli in the throat. In slightly more than one third of the cases the bacilli disappeared in one week, in 20 per cent in two weeks, in 16 per cent in three weeks and about 1 per cent became negative in the eighth, ninth and tenth week respectively. In isolated cases they persisted for fourteen and sixteen weeks.

Antihookworm Campaign

Hookworm infestation is common in the province of Corrientes and in the territories of Misiones, Chaco and Formosa, and on a lesser scale in certain districts of northern Santa Fe, Salta, Jujuy and Tucuman; isolated foci have been reported in other parts of the country, but the disease is prevalent only in the Northeast along the Paraná River. The national public health department and the provincial health departments have carried out a well planned campaign for several years. The surveys made by Professor Fülleborn and especially by Prof. Alois Bachmann laid the foundation for this work. Recently Dr. C. Fonso-Gandolfo, professor of infectious diseases in the University of Buenos Aires, made a tour of cities on the Paraná in Corrientes and the Chaco accompanied by several physicians and eighty students in two gunboats lent by the naval authorities. Indexes of infestation were made and numerous lectures on the prophylaxis of ancylostomiasis were delivered. Great publicity was given this survey during the fourteen days it lasted. Prophylaxis is being carried out by building sanitary latrines, periodic disinfestations and the education of the public in the use of shoes, as most people in the affected districts do not wear them. In other parts of the country, where shoes are usually worn, there is no hookworm infestation.

New Tuberculosis Hospital

The municipal authorities of the city of Buenos Aires have inaugurated a hospital for tuberculosis which has been built with a donation of 1,600,000 pesos (about \$465,000) made by F. Santojanni. The hospital will bear the donor's name.

Personals

Prof. D. Staffieri, incumbent of the chair of clinical medicine, has been elected dean of the medical faculty in Rosario.

Prof. Pio del Río Hortega has been invited to give a series of lectures and a practical course of normal and pathologic histology in the Medical School of the University of Buenos Aires.

ITALY

(From Our Regular Correspondent)

July 15, 1940.

Antituberculosis Vaccination

The presidents and directors of the antituberculosis centers of the various Italian provinces met recently at Rome on the occasion of the tenth antituberculosis crusade. The advisability of an early administration of preventive antituberculosis vaccines, especially in the first month of life, was generally admitted. It was resolved to give the vaccines systematically to nurslings in crèches as well as to those who are cared for in pediatric centers. The national institution for the protection of mothers and their infants as well as the General Center of Public Health gave instructions to the pediatric provincial centers of both the institution and of public health to give systematically antituberculous vaccination to newborn infants under the care of the centers.

Lecture on Syphilology

Prof. Lodovico Tommasi, who recently took charge of the chair of dermosyphilology at the University of Naples, in his opening lecture discussed the racial and demographic problems of syphilology. He defines race as the unity of moral and physical qualities and factors which are transmitted to the offspring and are perpetuated in the next generations according to genetic laws. So-called hereditary syphilis is congenital syphilis. Some believe that the living virus, syphilitic toxins and toxic syphilitic influences may taint the first, second and third generations. Still others believe in possible mutations of syphilitic toxins with the preservation of transmissible pathologic characters. Modern syphilology, however, does not admit hypotheses. The interpretation of the pathologic phenomena of syphilis is correct only when the spirochete is given the entire direct responsibility as the causal agent of the lesion. So-called parasymphilis, which is a coined word to express a prespirochetal phase, and the so-called syphilotoxins do not exist. Syphilis is one of the less toxic infections. Congenital syphilis is transmitted by the mother in the majority of cases. Syphilis in women may be of two types: the type which follows a course similar to syphilis in man and that which is not apparent, with no lesions showing the port of entry and without symptoms. The latter type is discovered through serologic tests for syphilis or by lesions of late appearance in rare cases. It shows more frequently in the offspring. The type of unapparent syphilis has been experimentally reproduced in animals by means of repeated inoculation with subinfecting doses. Congenital syphilis can be of the unapparent type and later on transmitted to the next generation. However, the transmission of syphilis to the third or fourth generation is exceptionally rare. In fact, it is not accepted by many syphilologists. According to modern knowledge congenital syphilis is acquired in intra-uterine life. The differential characters of congenital syphilis in relation to those of syphilis acquired during adult life depend on the tropism that the spirochete has for structures, including endocrine glands, during intra-uterine growth. They have no toxic dystrophic origin. However, in rare cases of congenital syphilis of the parents, especially parents with congenital syphilis of the first generation, a blastophthoria of Forel's type may taint the germinal cells and will result in the development of certain phenomena of dysplasia and dystrophy. The phenomena will appear later on, alone or in association with congenital syphilis. They are not influenced by antisymphilitic therapy. The speaker concluded that syphilis does not taint the race which remains insensible to the external attacks of the spirochete. Yet, from a demographic point of view, it causes much harm. The most recent Italian statistics show that congenital syphilis alone produces an annual rate of 30,000 deaths and that 10,000 are born with

one or several deficiencies. In association with acquired syphilis it causes an annual toll of 70,000 deaths and the presence in the country of about 750,000 syphilitic patients as sources of infection to the population.

Cinematography of the Larynx

Drs. Motta and Canova of Rome reported recently to the Accademia Medica of Rome the results of cinematographic researches on the larynx. They used an arc lamp placed beside the cinematographic apparatus in such a manner as to have the smallest angle between the luminous rays and the optic control of the objective. They carried on cinematography with the laryngoscopic mirror by this method. They registered the normal larynx of singers during the emission of vocal sounds, the larynx during phonation with the false cords and the vocal cords of persons with paralysis of a vocal cord or with some other diseases of the cords. The technic is simple.

Deaths

Prof. Giuseppe Sanarelli is dead. He was professor emeritus of hygiene at the University of Rome, of which he was ex-dean, Dr. ad honorem of the Universities of Paris and Tolosa, and professor of hygiene at the Universities of Bologna and Rome. Early in his professional life he wrote articles on his work at the Pettenkofer Institute in Munich and the Golgi Institute in Pavia and of his work with Pasteur in Paris. His work on immunity against anthrax contains two discoveries: the conception of opsonins and the introduction in the biologic technic of collodion sachets, which had an important development. Later at the request of the government of Uruguay he organized the Instituto de Higiene of Montevideo, where he carried on researches on yellow fever. He isolated *Bacterium icteroides*, the bacteria first found in the paratyphoid group. He discovered the virus myxomatosis in rabbits (*Sanarellia cuniculi*), a discovery which represents the cornerstone for the development of the history of filtrable viruses. He was deputy to the parliament in five legislatures and a senator.

Marriages

STANLEY C. USALIS, Kenilworth, Ill., to DR. MARGARET MARY VIDAS of Chicago in Windsor, Ont., Canada, July 14.

BROWN HUTCHESON CARPENTER, Danville, Va., to Miss Mary Harrison Vaughan of South Boston, June 29.

DAVID A. GERSHENSON, Fairfield, Ill., to Mrs. Lucille Pomeroy, of Carmi, in Reno, Nev., May 18.

ALBERT RITCHIE GILLESPIE, Charlottesville, Va., to Miss Louise Curtis of Ashok, N. C., May 25.

CLARENCE CONWAY BRISCOE, Philadelphia, to Miss Mary Elizabeth Suttle of Cynwyd, Pa., July 6.

HAROLD B. HENNING, Nashville, Tenn., to Miss Carolyn Prendergast of Chattanooga, June 28.

WILLIAM STONE HALL to Miss Oxena Elizabeth Gunter, both of Columbia, S. C., June 29.

ROBERT P. BOGNIARD, Ashland, Ohio, to Miss Mary Jane Nutter of Chesterhill, July 21.

JOHN BART LAURICELLA to Miss Dorothy Marie Donahue, both of New York, June 29.

ROBERT C. ORTON, New York, to Miss Edith Gersicoff of Rochester, N. Y., June 29.

OWEN F. PATTERSON, Springfield, Ohio, to Miss Mildred Senff of Wooster, June 11.

FLETCHER S. SLUDER JR., Danville, Pa., to Miss M. Orva Yost of Jeddo, June 30.

GEORGE S. BERGH to Miss Patricia Stephenson, both of Minneapolis, June 15.

DONALD BRINK, Isle, Minn., to Miss Margaret Johnson of Duluth, June 29.

MARVIN A. MITCHELL to Miss Nancy Stair, both of Atlanta, Ga., June 29.

Deaths

Arthur Stephen Hamilton, Minneapolis; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the Minnesota State Medical Association; Secretary of the Section on Nervous and Mental Diseases of the American Medical Association from 1915 to 1918 and 1920-1921; instructor of neuropathology from 1904 to 1912, clinical instructor and assistant professor of nervous and mental diseases from 1905 to 1912, associate professor from 1912 to 1916 and later professor, and director of the division of nervous and mental diseases, at the University of Minnesota Medical School; formerly professor of nervous and mental diseases at the University of Minnesota Graduate School; past president of the Hennepin County Medical Society, the Central Neuropsychiatric Association and the Minnesota Academy of Medicine; member of the American Neurological Association, American Psychopathological Association and the American Psychiatric Association; served during the World War; was on the staffs of the University, Swedish, Abbott, St. Andrew's, St. Mary's, Fairview, Asbury and Northwestern hospitals; aged 67; died, June 2, of arteriosclerosis and encephalomalacia.

Eben Clayton Hill Ⓢ Captain, U. S. Army, retired, Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1907; entered the medical corps of the U. S. Army as a first lieutenant in 1909 and retired as a captain in 1913 for disability in line of duty; assistant in anatomy, 1907-1908, instructor, 1920-1921, and associate in anatomy, 1921-1922, at his alma mater; for many years on the staff of the Vassar Hospital and Dispensary, Poughkeepsie; fellow of the American College of Physicians; aged 58; died, June 15, in the Burbank Hospital, Fitchburg, Mass., of coronary thrombosis.

David Perla Ⓢ New York; Columbia University College of Physicians and Surgeons, New York, 1923; member of the American Association of Pathologists and Bacteriologists and the American Society for Experimental Pathology; an instructor at his alma mater; co-author, with Dr. Jessie Marmorston, of "Spleen and Resistance"; aged 39; since 1927 associate pathologist and bacteriologist on the staff of the Montefiore Hospital, where he died, June 14, of rheumatic heart disease.

William Henry Donnelly, Brooklyn; McGill University Faculty of Medicine, Montreal, Que., Canada, 1903; assistant professor of pediatrics at the New York Post-Graduate Medical School and Hospital, New York, from May 1924 to June 30, 1934; appointed instructor in pediatrics in June 1920 and associate in pediatrics in June 1922; aged 58; died, June 22, in a hospital at Montreal, Que., Canada, of hypertension and myocarditis.

George Leman Collins Ⓢ Medical Director, United States Public Health Service, retired, Washington, D. C.; Harvard Medical School, Boston, 1900; served as a first lieutenant in the Medical Corps of the U. S. Army in 1902; entered the United States Public Health Service in 1903 and retired in 1933; fellow of the American College of Surgeons; aged 66; died, June 17, in the Emergency Hospital, of acute dilatation of the heart.

Andrew Frank Richards, Sparta, Tenn.; University of Tennessee Medical Department, Nashville, 1893; member and past president of the Tennessee State Medical Association; member of the House of Delegates of the American Medical Association, 1917-1918; served during the World War; for many years a member of the state department of public health; aged 74; died, June 14.

Thomas Bray Spence Ⓢ Brooklyn; College of Physicians and Surgeons, medical department of Columbia College, New York, 1893; fellow of the American College of Surgeons; served during the Spanish-American and World wars; attending surgeon to the Methodist Episcopal Hospital; consulting surgeon to St. John's Hospital; aged 72; died, June 19, of heart disease.

Joseph Sidney Morrison, Royal Oak, Mich.; Detroit College of Medicine, 1905; member of the Michigan State Medical Society; past president of the Oakland County Medical Society; for many years member of the board of education; aged 63; died, June 20, in the Oakland County Tuberculosis Sanatorium, Pontiac, following an operation for a pulmonary cyst.

Eugene George Kessler, New York; Columbia University College of Physicians and Surgeons, New York, 1898; member of the Medical Society of the State of New York; for many years consulting physician to the dispensary of the Lenox Hill Hospital; aged 73; died, June 20, of carcinoma.

J. Spencer Callen, Shenandoah, Pa.; College of Physicians and Surgeons, Baltimore, 1881; member of the Medical Society of the State of Pennsylvania; past president of the Schuylkill County Medical Society; for many years president of the board of education; aged 86; died, June 4, of senility.

Lloyd Edress Oaks Ⓢ Twin Falls, Idaho; Jefferson Medical College of Philadelphia, 1930; member of the Pacific Coast Oto-Ophthalmological Society; on the staff of the Twin Falls County General Hospital; aged 37; died, June 10, in a hospital at Denver of pulmonary tuberculosis.

Charles Francis King, McKeesport, Pa.; Medico-Chirurgical College of Philadelphia, 1910; member of the Medical Society of the State of Pennsylvania; aged 55; died, June 22, in the Graduate Hospital of the University of Pennsylvania, Philadelphia, of carcinoma of the bladder.

John Henry Jones, Dowagiac, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1893; member of the Michigan State Medical Society; for many years member of the board of education and city physician; aged 80; died, May 24.

James Wilcox Turner, Cedar Keys, Fla.; Medical Department of Tulane University of Louisiana, New Orleans, 1904; at one time acting assistant surgeon in the United States Public Health Service; formerly state senator; aged 62; died, June 21, of carcinoma of the prostate.

Frederick Clarence Hanmore, Chicago; Bennett College of Eclectic Medicine and Surgery, Chicago, 1906; member of the Illinois State Medical Society; police surgeon; aged 57; died, June 17, in the Wesley Memorial Hospital of pulmonary embolism and lung abscess.

Guy William Henika, Madison, Wis.; Harvey Medical College, Chicago, 1897; member of the State Medical Society of Wisconsin; deputy state health officer; formerly assistant state health officer; aged 69; died, June 8, of injuries received in an automobile accident.

Norman M. Johnson, Durham, N. C.; Washington University School of Medicine, Baltimore, 1877; member of the Medical Society of the State of North Carolina; formerly county health officer and county coroner; aged 87; died, June 13, of heart disease.

Alfred Anthony Keller, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1910; member of the Louisiana State Medical Society; on the staff of the Charity Hospital; aged 52; died, June 14, of coronary thrombosis.

Daniel Garver Kuhlthau Ⓢ New York; Columbia University College of Physicians and Surgeons, New York, 1926; member of the American Academy of Dermatology and Syphilology; aged 39; died, June 3, in the New York Post-Graduate Hospital.

Augustus Frederick Kober Ⓢ Charles City, Iowa; University College of Medicine, Richmond, 1901; Northwestern University Medical School, Chicago, 1902; on the staff of the Cedar Valley Hospital; aged 65; died, June 6, of cirrhosis of the liver.

Joshua Raymond Storie, Cookeville, Tenn.; University of Tennessee Medical Department, Nashville, 1894; also a lawyer; formerly Fentress county judge and chairman of the board of education; aged 85; died, May 9, of chronic myocarditis.

Louis Andrew Derry, Portland, Maine; Medical School of Maine, Portland, 1906; member of the Maine Medical Association; fellow of the American College of Surgeons; on the staff of the Queen's Hospital; aged 60; died, June 16, of heart disease.

Harry Ernest Heinitsh Jr., Spartanburg, S. C.; Jefferson Medical College of Philadelphia, 1918; member of the South Carolina Medical Association; aged 45; on the staff of the Spartanburg General Hospital, where he died, June 20, of typhus fever.

Marion Ernest Quina Ⓢ Pensacola, Fla.; Medical Department of Tulane University of Louisiana, New Orleans, 1905; served during the World War; aged 57; on the staff of the Pensacola Hospital, where he died, June 12, of carcinoma of the lung.

Sam Harmon Taylor Ⓢ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1924; served during the World War; aged 41; on the staff of the Santa Rosa Hospital, where he died, June 3, of coronary thrombosis.

Frank H. Garverich, Harrisburg, Pa.; University of Maryland School of Medicine, Baltimore, 1888; Jefferson Medical

College of Philadelphia, 1891; formerly county physician; aged 78; died, June 15, of arteriosclerotic renal disease.

Lawrence C. Nell, Gradyville, Ky.; Kentucky School of Medicine, Louisville, 1891; formerly state senator and state representative; aged 72; died, June 21, in the T. J. Samson Community Hospital, Glasgow, of cerebral hemorrhage.

Isidore Rutherford Lowenthal, New York; Memphis (Tenn.) Hospital Medical College, 1897; lunacy commissioner for New York County, 1926-1927; aged 67; died, June 3, in the Beth Israel Hospital of chronic myelogenous leukemia.

George Elbert Adams, Jacksonville, Fla.; Medical College of the State of South Carolina, Charleston, 1911; member of the Florida Medical Association; for many years county physician; aged 55; died, June 11, of coronary thrombosis.

John Robert Andrew Lang Jr., Reno, Nev.; Cornell University Medical College, New York, 1921; member of the Nevada State Medical Association; served during the World War; aged 43; died, June 1, of coronary thrombosis.

Manly Dufferin Caughey, Detroit; Michigan College of Medicine and Surgery, Detroit, 1905; member of the Michigan State Medical Society; aged 64; died, June 12, in the Harper Hospital of lobar pneumonia and myocarditis.

James Nelson Gill, Weaverville, N. C.; Vanderbilt University School of Medicine, Nashville, Tenn., 1889; formerly mayor and health officer; aged 78; died, June 5, in a hospital at Asheville of uremia and chronic nephritis.

Frank Albert King, New York; Long Island College Hospital, Brooklyn, 1899; surgeon in the United States Public Health Service reserve; served during the World War; aged 67; died, June 13, of coronary thrombosis.

Leslie Eugene Kelton Sr., Corsicana, Texas; University of the South Medical Department, Sewanee, Tenn., 1897; on the staff of the Physicians and Surgeons Hospital; aged 70; died, June 19, of coronary occlusion.

James C. Norris, Augusta, Ky.; Homeopathic Hospital College, Cleveland, 1884; member of the Kentucky State Medical Association; aged 80; died, June 13, in the Hayswood Hospital, Maysville, of myocarditis.

Michael Robinson, San Francisco; Kentucky School of Medicine, Louisville, 1904; aged 67; died, May 3, in the Veterans Administration Facility of cerebral hemorrhage, arteriosclerosis and hypertension.

John Thomas William Rowe, New York; Bellevue Hospital Medical College, New York, 1885; member of the Medical Society of the State of New York; aged 81; died, June 7, of heart and renal disease.

Moses H. Clagett, Berea, Ky.; University of Louisville Medical Department, 1887; formerly mayor of Menno, S. D.; aged 79; died, June 10, in the Berea College Hospital of cardiovascular disease.

Warren D. Cline, Williamstown, W. Va.; Eclectic Medical Institute, Cincinnati, 1886; aged 83; died, June 5, in the Marietta (Ohio) Memorial Hospital of diabetes mellitus and coronary occlusion.

Beuhler B. Richmond, Skelton, W. Va.; Louisville (Ky.) Medical College, 1901; member of the West Virginia State Medical Association; aged 64; died in June of myocarditis and cerebral sclerosis.

Charles P. Cook, Ennis, Texas; Memphis (Tenn.) Hospital Medical College, 1895; on the staff of the Municipal Hospital; aged 68; died, June 14, of cerebral embolus and coronary occlusion.

Jasper Lee Jackson, Manchester, Ga.; Atlanta College of Physicians and Surgeons, 1902; member of the Medical Association of Georgia; aged 69; died, June 2, in a hospital at Atlanta.

Andrew Rufus Howell, North Little Rock, Ark.; Jefferson Medical College of Philadelphia, 1887; member of the Arkansas Medical Society; aged 76; died, July 19, of intestinal obstruction.

Harriet V. Bills Brooks, River Rouge, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1877; aged 89; died, June 7, of acute dilatation of the heart.

Samuel Oscar Wilder, Chatham, La.; Louisville (Ky.) Medical College, 1884; formerly member of the state legislature, postmaster and bank president; aged 83; died, May 2.

William C. Hale Jr., Dallas, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1896; formerly county health officer; aged 64; died, June 12.

Charles F. Wharton, Richmondville, N. Y.; Albany Medical College, 1883; for many years health officer; aged 77; died, May 25, in the Parshall Private Hospital, Oneonta.

Isaac William Brown, Jackson, Miss.; Meharry Medical College of Walden University, Nashville, Tenn., 1905; aged 71; was shot and killed, June 21, by an unknown assailant.

Edgar Morgan Webster, Chicago; Starling Medical College, Columbus, 1884; formerly on the staff of the South Chicago Community Hospital; aged 80; died, May 9.

Boston H. B. Grayston, Huntington, Ind.; Chicago Medical College, 1875; member of the Indiana State Medical Association; aged 90; died, June 19, of pulmonary edema.

Ira Hamilton Miller, Louisiana, Mo.; Missouri Medical College, St. Louis, 1899; served during the World War; aged 63; died, June 6, of a self-inflicted bullet wound.

C. T. McDonald, Idabel, Okla.; Hospital College of Medicine, Louisville, Ky., 1905; aged 70; died, June 9, of carcinoma of the liver, hypertension and diabetes mellitus.

Allen Chapman Brown, Stanwood, Wash.; Missouri Medical College, St. Louis, 1895; member of the Washington State Medical Association; aged 76; died, May 18.

Richard Adolphus Harkins, Fort Smith, Ark.; University of Nashville (Tenn.) Medical Department, 1907; served during the World War; aged 59; died, May 16.

Max Feldman, Chicago; St. Louis College of Physicians and Surgeons, 1918; Chicago Medical School, 1922; aged 52; died, June 5, in an automobile accident.

Harold Austin Kraiss Mingle, Blue Ball, Pa.; Temple University School of Medicine, Philadelphia, 1927; aged 40; died, June 21, of coronary embolism.

James Allen Cotton, Peoria, Ill.; (licensed in Illinois in 1899); aged 71; died, June 10, in the Methodist Hospital of bronchogenic carcinoma of the lung.

Clark Le Roy Warren, Hines, Ill.; Rush Medical College, Chicago, 1897; aged 69; died, June 25, in the Veterans Administration Facility of tuberculosis.

Warren T. Chase, Loup City, Neb.; Hahnemann Medical College and Hospital, Chicago, 1882; aged 80; died, June 12, of cardiovascular disease.

Howard M. Holverson, Boise, Idaho; Hahnemann Medical College and Hospital, Chicago, 1901; aged 66; died, May 20, of coronary thrombosis.

Perry Smith Holmes, Mountain Pine, Ark. (licensed in Arkansas in 1903); aged 67; died, June 20, of myocarditis, influenza and nephritis.

Amos Flint Blanchard, Jamestown, N. Y.; University of Buffalo School of Medicine, 1888; aged 75; died, June 1, of coronary thrombosis.

Ethelbert Reavley, Spirit River, Alta., Canada; McGill University Faculty of Medicine, Montreal, Que., 1887; aged 79; died, April 28.

J. Hermenegilde Raymond, Lyster Station, Que., Canada; Laval University Faculty of Medicine, Quebec, 1911; aged 54; died in April.

Kee Wakefield, Minneapolis; University of Wooster Medical Department, Cleveland, 1869; Civil War veteran; aged 97; died, May 8.

Robert Edgar Buswell, Calgary, Alta., Canada; University of Toronto Faculty of Medicine, 1908; aged 59; died, April 15.

Rufus A. Vaughan, St. Louis; University of Nashville (Tenn.) Medical Department, 1872; Civil War veteran; died, May 24.

Louis H. Wheeler, Tully, N. Y.; Baltimore Medical College, 1901; for many years health officer; aged 62; died, May 15.

Oscar A. Kent, Huntington, W. Va.; Baltimore Medical College, 1895; aged 69; died, June 14, of cerebral hemorrhage.

David Roland Livingstone, Melville, Sask., Canada; Trinity Medical College, Toronto, Ont., 1900; died, May 18.

Hal Sewell Armistead, Atlanta, Ga.; Memphis (Tenn.) Hospital Medical College, 1909; aged 52; died, May 12.

Robert S. Short, Garner, Ky. (licensed in Kentucky under the exemption law of 1885); aged 83; died, May 19.

Isaac D. Benson, Anguilla, Miss.; Memphis (Tenn.) Hospital Medical College, 1898; aged 67; died, May 11.

Jessie T. Knight, Ravenna, Texas; (licensed in Texas, under the Act of 1907); died recently.

S. S. Holtz, Plymouth, Ohio; Pulte Medical College, Cincinnati, 1877; aged 88; died, June 7.

Ernest Henry Cole, St. Louis; St. Louis Medical College, 1885; aged 82; died, May 22.

Bureau of Investigation

AN ELECTRICAL ENGINEER BLOWS A FUSE

Short Circuit in Pseudomedical Line Followed by Post Office Fraud Order

In the thirty-four years that the Bureau of Investigation has been functioning, farmers and mechanics, housewives and others who should know better have been found associated with the sales of "cures." Occasionally even scientists of standing in their own fields have not hesitated to encroach on that of medicine by proclaiming the "discovery" or development of some alleged miracle of healing. Typical is the case of Louis Bond Cherry of El Paso, Texas, said to be a retired electrical engineer.

Cherry first came to the attention of the American Medical Association through a booklet written in fanciful style on his "Neuropo System of Restoring Health." This consisted of a chief nostrum "Neuropo" and supplementary products which, used singly or in combination, were represented to help bring about "rejuvenation" and to cure or relieve a wide variety of disorders. Among these were paralysis, locomotor ataxia, gonorrhea, prostatitis, pulmonary tuberculosis, pneumonia, diphtheria, mumps, chicken-pox, scarlet fever, tapeworm, asthma, bronchitis, eczema, moles, warts, indigestion, blood poison, diabetes, pyorrhea, anemia, neurasthenia, pleurisy, neuralgia and even baldness.

Another advertising booklet, put out later by Cherry, was written, he said, "just a little past three A. M." on his fifty-third birthday:

Must I speak and lay bare to the world those things which are ordinarily considered personal and kept secret?

After a long barrage of fantastic language he reached this firm resolve:

Yes, I WILL DO IT! At last, I MUST AND WILL SPEAK! . . . For me to withhold the story of how I restored myself to health from the curse of disease, and how I became rejuvenated in an unbelievable measure, endowed with enabling vitality to work as high as eighteen hours a day could not be but considered a crime of omission against humanity, for which I could never hope to receive forgiveness or peace of mind. Though, dear reader, it may mean sore persecution for me from those whose "organized practices" such a simple and revolutionary discovery might financially disturb, NEVERTHELESS, I WILL TELL YOU MY STORY.

Skipping a few more vagaries, one comes to the more personal parts of Cherry's life story. From his boyhood on a Kansas farm, where he enjoyed a "rugged constitution and high vitality," he goes on to his career in the city, where, he relates, he worked in a machine shop, a factory and a power house "gaining the practical experience in electrical and mechanical engineering" and also pursuing the study of chemistry, electrochemistry, biochemistry and medicine! These activities, he says, depleted his energy, and an attack of influenza in 1918, followed by two attacks of pneumonia, left him with "a well defined case of tuberculosis." And then:

As though in confirmation of the old saying, that "It never rains but it pours," I received from the hand of Fate, who wielded the razor while getting shaved, a cut on the upper lip, from which developed a syphilitic infection, which unfortunately was not discovered as such until the disease had progressed in my system for about three weeks. Alarmed beyond words at my plight, I sought the best medical advice I could get, and began taking "shots" of 606 or similar arsenical preparations, following each course of six with six shots of mercury, taking in all sixty of such dosages (thirty of each) until I began to wonder which I would ultimately

evolve into, a thermometer or a barometer. During all of this time of medical treatment I could feel myself slipping toward the open grave, as it seemed, and from which there seemed no possible way of escape. I sought and consulted medical practitioners, "specialists" in their line, and received but the one general answer to my queries to the effect that "there was no cure for tuberculosis or syphilis; that it could only be suppressed."

Thus the services of medical science seem to have suspended entirely during Cherry's quest for relief. In fact, he adds:

Depressed at the failure of the doctors to give me even temporary relief, or encouragement, I became desperate and concluded to attempt the compounding of a remedy for my tuberculosis as that was the disease which seemed the most serious, or, at least, caused me the greatest suffering and exhaustion.

As a drowning man will grasp at a straw, so Cherry took up with—of all things—what he calls the electron theory! But so did Albert Abrams and George Starr White and some other promoters of fantastic methods in medicine. And there, of course, "vibrations" enter the picture, together with "color waves." But what have these to do with "patent medicines"? Well, Cherry found in some book that the "value of any medicine or drug as a remedial agency depended upon the DIS-ENGAGEMENT OF ENERGY IN THE HUMAN BODY CORRESPONDING TO ITS COLOR WAVE. Not that the energy was disengaged as COLOR, but as ENERGY. COLOR BEING SIMPLY THE TRADE MARK OF NATURE, by which different wave lengths of energy may be recognized."

And, further, according to Cherry, the discovery of this theory "marked the dawn of a new era in the treatment of disease." In fact, he says:

It was this discovery, we are told, that led into the development of treating disease by specific wave lengths of light—chromotherapy. It was also the source of inspiration which led me into research work which resulted in the development of our present "Neuropo System of Restoring Health."

But Cherry must have realized that it is hard to sell an abstract idea alone, for after a series of circumlocutions he finally got down to the business of adapting the theory to something salable. He did not believe, he said, in administering drugs, chemicals or serums, but he did advocate such things as "spinal adjustments and manipulations . . . with an alkaline bath once or twice a day followed by an external application of a proper alkaline protein preparation to the back, abdomen and chest to reduce acidosis and equalize the nerve potential . . ." He determined that his mixture must be something nonpoisonous, readily absorbable and noninterfering with bodily functions:

In other words, I believed that I must produce a chemical compound with all of the wave length characteristics necessary to kill tubercle bacilli, and at the same time have it so harmless that one could take a bath in it several times daily, if so required, without any harmful results . . . and therefore it was evident to my reasoning that to cure tuberculosis and other diseases we must neutralize the acid condition or in other words alkalize the system. I therefore concluded that some form of alkaline protein or albuminoid compound would more correctly imitate nature in combating disease.

It might seem unthinkable to ordinary scientists to be able to crowd chromotherapy and wavelengths into a bottle that was already filled with "some form of alkaline protein or albuminoid compound"—but leave it to Cherry. Was he not a trained engineer? Here is part of his secret:

Thus did I reason and work, trying this and that combination of chemicals and drugs—making spectographs of the various compounds, emulsions and colloidal combinations, comparing them with the picture of the spectrum of the tubercular culture, testing the different samples on my skin in order to study its effect, ability to penetrate or be absorbed, which tests were often followed by dumping the whole batch into the sewer to try something else . . . until I succeeded in getting a compound that would relieve my cough temporarily . . . just in time, as I was beginning to lose all hope of accomplishing anything worth while.

And, of course, there followed "an increase in pep and vitality" (familiar words!) which, however, was succeeded in turn by a temporary relapse. Perhaps he had not put in enough chromotherapy and wavelengths. This thought may also have occurred to Cherry, for, in spite of some subsequent improvement in his condition:

I began again my experiments in modifying the remedy . . . About six weeks after I began treating myself, I had improved to such an extent that I suspected the remedy was improving my syphilitic condition and accordingly had a Wassermann test made. Although I had no idea at first that it would be effective in this disease, I found the test negative.



Electrical engineer Louis Bond Cherry.

But Cherry had still more to contend with:

In addition to being afflicted with tuberculosis and syphilis . . . I found that I also had cancer of the sigmoid . . . and I naturally felt somewhat depressed by this added complication. The treatments I had been taking did not seem to be helping my cancer trouble . . . so I concluded to make a local application of the remedy diluted with warm water . . . applied as a high enema . . . followed by the application of an ointment made from the same ingredients as the remedy (except in different proportions) to which was added a little yellow iodid of mercury . . . cocoa butter and an oil. . . These treatments were . . . supplemented with a diet of fruit juices, sauerkraut, vegetables, and very little meat.

After treating himself thus for a few days, Cherry says, he passed with stool "what appeared to be a tumorous growth consisting apparently of fibrous mucous tissue, mixed with pus and blood." Successive treatments "seemed to completely eradicate all symptoms of cancer and I have never been troubled with it since and 'Radionic' diagnosis shows zero reaction." [Some Abrams stuff.—Ed.]

But Cherry is at his quaintest in summing up his experiences:

To bring the story of my fight for life to a close, one year after I first began treatment for tuberculosis, I was able to pass most known tests that science considers as more or less reliable (including the E. R. A. or electronic test) [Some more Abrams stuff.—Ed.] which found all diseases with which I had been afflicted were of negative indication.

The Q. E. D. of Cherry's thesis, therefore, is that for cancer, tuberculosis, and all the rest of the category, the answer is his Neuropo or Neuropo Ointment, or both. As supplementary treatments one may take Neuropo enemas, baths and douches. The name Neuropo, incidentally, he says, "is evolved from the Latin NEURO POTENS, signifying *nerve power*, which is unquestionably built up by its use . . ." Although Cherry advises the reader to "use Neuropo for all ailments" and goes on to name a long list of more or less serious conditions in which he recommends its use, he finally admits:

We do not claim to have discovered the "Elixir of Life" or the "Fountain of Perpetual Youth" . . . but we do believe that in our NEUROPO SYSTEM OF RESTORING HEALTH . . . we have possibly advanced our knowledge and understanding of the science of living to such an extent that others following . . . may make further contributions, to the end that we as a race shall be able to extend our lives many years, on and on,—even to the ultimate expectancy of "Everlasting Life"—HERE ON EARTH.

It is at least a beautiful thing to hope for,—a vision so resplendent with expectation and alluring in its scope that the much heralded picture of a future life beyond the grave seems to fade or dissolve into the possible "Reality" of prolonged joys of living HERE. With a brand new body every seven years, properly maintained and kept normally alkaline, one should never get to be in reality, over seven years of age according to the scientific view.

To those persons who have lived a long time but have never been "over seven years of age" Cherry's ideas should make an irresistible appeal!

But all was not to be smooth sailing for Cherry's venture in the sale of bottled wavelengths, chromotherapy and Neuropo. The Post Office Department, for one, became skeptical of his claims. It learned that his business was started in Kansas City but was moved to El Paso in February 1932. Though Cherry claimed that it was incorporated in Texas, he was unable to furnish the date of incorporation, and it appeared that he was the only person connected with the enterprise, as he operated it from his home and had no employees, it was said. He obtained business by sending out printed circulars, a booklet and specially prepared letters to those whose names he got in various ways. As he refused to give the Post Office inspectors the formulas for his several preparations, these products were purchased through the mails and analyzed by a government chemist, whose condensed reports follow:

NEUROPO: Ammonia, 18 per cent; potassium sulfate, iron and magnesium; volatile oils (including saffrol); fatty (saponifiable) material; alkaloidal (?) material; proteins (claimed on label) present, but in very small amount; no mercury, salicylates, or iodides.

NEUROPO BATH LOTION: Ammonia, 18.7 per cent; potassium sulfate, with magnesium and iron; volatile oils (saffrol and turpentine indicated); saponifiable fats and oils.

NEUROPO OINTMENT: Xylene; sodium carbonate, chloride and iodide; volatile oil (turpentine-like); fatty acids (calculated as oleic); saponifiable fats; mercury and iodine (probably as mercuric iodide in original); triethanolamine (an emulsifying agent) and gum indicated in small amounts; yellow fluorescent dye present; amount of protein (mentioned on label) insignificant.

NEUROPO ENEMA SOLUTION: Ammonia, less than 1 per cent; iron, magnesium, potassium and sulfates; volatile oils (such as turpentine); fatty oils; gum indicated in very small amount.

NEUROPO DOUCHE SOLUTION: Ammonia, less than 1 per cent; magnesium, potassium, sodium and sulfates; volatile oils (such as turpentine); fatty material; yellow dye with strong green fluorescence present; gum indicated in very small amount.

The Post Office memorandum on this case brought out that expert medical testimony showed the worthlessness and in some cases the actual harmfulness in using these nostrums for the conditions named.

In his written reply Cherry appears to have dodged the specific charges, but he claimed that in addition to his "medicine" business he was also engaged in some chemical research work of a nonmedical type which would be hampered if a fraud order was issued against the names he used in his nostrum business. As he did not, however, offer to discontinue making and selling his "patent medicines," and as his claims for them were found "grossly fraudulent," the Post Office issued a fraud order against the names Louis Bond Cherry, Louis Bond Cherry Office and Laboratories, Cherry Laboratories and Neuropo Products Company, on Aug. 10, 1939.

In that summer Cherry had also run into trouble from another direction. The El Paso Herald-Post for July 12, 1939, reported that Louis Bond Cherry had been found guilty of violating state laws in falsely labeling one of his products (in that article spelled "Neu-Ro-Pro") and fined \$200 and costs in a local court. The report further stated that Cherry was facing trial on a second complaint, this one involving his ointment, but that the trial would be postponed pending outcome of his appeal on the first complaint.

So much for the spectacle of an individual who, after shifting from engineering to pseudomedicine sputtered feebly until put out by the Post Office Department.

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act and in cases in which they refer to drugs and devices they are designated D. D. N. J., cosmetics C. N. J., and foods F. N. J. The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the composition; (4) the type of nostrum; (5) the reason for the charge of misbranding and (6) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

Andree Eye Lash and Brow Color.—Andree Laboratories, Coatesville, Pa. Composition included paraphenylenediamine. Declared potentially injurious if used as directed.—[C. N. J., F. D. C. 11; May 1940.]

Dark Eyes.—Dark Eyes, Chicago. Composition included ammoniated silver nitrate and pyrogallol. Eyelash and brow dye. Declared potentially injurious if used as directed.—[C. N. J., F. D. C. 12; May 1940.]

Hollywood Lash and Brow Dye.—Hollywood Lash Dye Co., Hollywood and Los Angeles. Composition included paraphenylenediamine. Declared potentially injurious if used as directed.—[C. N. J., F. D. C. 7 and 8; May 1940.]

Ideal Lash and Brow Dye.—George W. Eilert trading as the Ideal Lash & Brow Co., Los Angeles. Composition included paraphenylenediamine. Declared potentially injurious if used as directed.—[C. N. J., F. D. C. 10; May 1940.]

Lash Lure.—Lash Lure Cosmetic Manufacturing Co. or Cosmetic Manufacturing Co., Los Angeles. Composition included paraphenylenediamine. Eyelash and brow dye. Declared potentially injurious if used as directed.—[C. N. J., F. D. C. 1 and 2; May 1940.]

Mary Luckie Improved Lash and Brow Dye.—Mary Luckie, Inc. (No address given.) Composition included paraphenylenediamine. Declared potentially injurious if used as directed.—[C. N. J., F. D. C. 9; May 1940.]

Miller's Anti-Mole.—Miller Manufacturing Co., Lincoln, Neb. Composition included nitric acid . . . g warts and moles. Declared potentially injurious . . . N. J., F. D. C. 18 and D. D. N. J., F. D. C. 71; May 1940.]

Palmer's Antiseptic Skin Lotion.—Solon Palmer, New York. Contained corrosive sublimate. For eczema, pimples, dandruff and itching, scaly eruptions. Declared potentially injurious if used as directed.—[C. N. J., F. D. C. 68; May 1940.]

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

HEAT SENSITIVENESS

To the Editor:—For the past year a youth aged 19 years has developed giant urticaria following sweating after physical exertion. The wheals appear first around the belt line and then may develop on any part of the body. They grow to enormous size and thickness and usually disappear within twenty-four hours. Epinephrine seems to affect them but little. His health is excellent. What are the possible causes of this condition and the treatment?

M.D., California.

ANSWER.—Occasionally patients possessing thermic or heat sensitiveness may have reactions in the form of urticaria produced by increases of temperature which are sometimes of slight degree and produced by mental or physical effort; this type is called urticaria calorica to distinguish it from the urticaria of contact reactions. Symptoms of itching of the skin with or without wheal formation occur in such cases particularly when the body temperature is subnormal; they can be prevented by the application of cold.

Treatment is at times even more difficult than diagnosis. The mild case is often relieved by simply avoiding those situations which have been found productive of symptoms. For those who react either to heat or to cold, Duke has found that therapeutic alternation of the extremes of temperature may increase tolerance to a high degree. For example, treatment is begun with a hot water bottle or small bulb at some distance and, as soon as the patient reacts, cold is applied. When symptoms are relieved, heat is again applied. This is alternated several times at each treatment. The degree and duration of heat exposure are gradually increased until the patient can tolerate, if possible, prolonged exposure to the heat of a 1,500 watt lamp.

Caven used diathermy with elevation of temperature to 104 F. biweekly with good results. Temperature raising substances, e. g. colon or typhoid vaccine, are used. The use of epinephrine has been disappointing.

RECOVERY FROM TROPICAL DISEASES

To the Editor:—If a man has contracted malaria, amebiasis, schistosomiasis, filariasis, kala azar or hookworm disease in a tropical country and leaves that country permanently and returns to a cool nontropical country so that he has no opportunity for reinfection or reinfestation, how long will it take for the disease to die out with and without treatment? I have consulted textbooks on parasitology and helminthology and have been unable to find this information.

M.D., New York.

ANSWER.—Untreated patients with malarial infections have been known to harbor the parasites for several years in localities where there is no opportunity for reinfection. The length of time the infection will last is probably determined by the age, race and resistance of the patient, and the virulence and species of parasite involved. Therefore it would be impossible to determine in advance just how long any patient would retain his infection. With proper treatment many such patients are completely cured, but it must be remembered that even prolonged treatment by any of the antimalarial drugs now known may in some cases succeed only in keeping down clinical attacks without eliminating the parasites. It is not uncommon for patients to show relapses at varying periods of time following even intensive antimalarial therapeutics.

Patients having active amebiasis may become carriers, may pass into the chronic state or may become spontaneously cured. Again, as in the case of malaria, many variables are involved which are not yet well understood. It is not infrequent to encounter examples of chronic amebic dysentery which have persisted for twenty years. Modern treatment greatly improves the chances for complete cure, but again it should be pointed out that treatment may bring about a disappearance of symptoms without effecting a complete cure.

Schistosome worms are long lived in the human patient. Even mild infections may last ten years, and infections of thirteen years' duration are known. Spontaneous cures are rare except in cases in which the number of worms is small. Intensive treatment is necessary to effect a cure. The efficacy of the drugs most commonly used depends on their ability to prevent egg production in the female worm. This may be effected temporarily in some cases, with a return of normal egg production

when the treatment has been discontinued too soon. Although there are no definite data on the longevity of adult filaria, it is known that they can live a long time in man. The worms require a year to reach maturity, so it is reasonable to believe that they live several years. No effective treatment is known.

A high percentage (from 90 to 95) of untreated cases of kala azar terminate fatally. The duration is variable, from a few months for acute cases to two or three years for chronic cases. Patients have been known to retain the infection for five years. Treatment is now so satisfactory that the great majority of patients are cured. However, relapses following treatment are not unknown.

Hookworms can live for as long as from four to eight years in the intestine of man. However, studies on prisoners who were not subjected to reinfection have shown that a large number of the worms are lost in from six months to a year. Since hookworm treatment usually does not remove all the worms, the latter may persist for some time after treatment with the best available drugs. However, since they cannot multiply in man, a complete cure can usually be obtained by repeated treatments.

PLANTAIN, HOUSE DUST AND BACTERIAL ALLERGY

To the Editor:—A young woman presented herself during the grass pollen season for treatment because of violent coughing spells, which had existed since January 1940 following an attack of influenza and sinusitis. There is a history of cough during the preceding summer, which apparently began and ceased with the onset and cessation of the grass season. The pulmonary examination is essentially negative. The sinuses are clearing up under treatment. X-ray examination reveals thickening of the mucous membrane of the sinuses. Cutaneous tests give a 3 plus reaction to house dust 1:1,000 and to plantain 1:1,000. A vaccine made from the purulent nasal discharge doesn't give a local skin reaction but gave a slight systemic reaction such as sneezing and stuffiness of the nose and aggravated the cough for about thirty minutes. Would it be advisable to give the house dust and plantain and vaccine subcutaneously now? How could one proceed to use these materials so that, should on unfavorable reaction occur, one would know which one was the causative factor? The positive food allergens have been eliminated. In a case of this sort would there be any objection to using displacement therapy with 0.25 per cent ephedrine sulfate solution for treatment of the infected ethmoid?

M.D., Pennsylvania.

ANSWER.—The impression gained is that the patient's symptoms may be the result of a combination of extrinsic allergy and bacterial infection, and possibly allergy to the bacteria. When the inquirer speaks of the grass season it is presumed that he is referring to the plantain season, since no mention is made of positive reactions to grass pollens. There is no clearcut clinical evidence for house dust allergy, although the possibility of the presence of the latter has not been disproved. The systemic reactions from the vaccine injections speak strongly in favor of an allergy to these bacteria. Considering the facts presented, it would seem advisable to treat the patient with subcutaneous injections of all three materials: plantain pollen extract, house dust extract and the bacterial vaccine. Ordinarily all three antigens can be administered at one visit. However, if constitutional reactions tend to repeat, it may be necessary to give each material on a separate visit in order to locate the particular one responsible for the reaction. In most instances also the antigen responsible for constitutional symptoms is the one giving the most marked local reaction. There is no particular objection to the use of ephedrine displacement therapy, although simple vacuum aspiration may be just as effective.

TREATMENT OF PARKINSON'S DISEASE

To the Editor:—Will you please let me know the latest treatment for paralysis agitans and whether vitamin B is of special value.

T. J. Jensen, M.D., Duluth, Minn.

ANSWER.—With regard to the treatment of Parkinson's disease or true paralysis agitans, Oppenheim remarked "In this disease the physician can do much harm and little good." Since the actual cause is unknown, any treatment is of necessity purely symptomatic. That the lesion is a degenerative one associated with cerebral vascular sclerosis involving the lenticular nucleus and its related structures is well founded at this time. Some of the symptoms may be alleviated by carrying out passive movements by giving tepid baths or by the use of mild vibration massage. Scopolamine hydrobromide in doses of from $\frac{1}{100}$ to $\frac{1}{500}$ grain (0.0004 to 0.00065 Gm.) three or four times daily by mouth may be used. Powdered stramonium leaves in doses of from $\frac{1}{12}$ to 2 grains (0.1 to 0.13 Gm.) three or four times daily. The tincture of stramonium may be given in doses of from 15 to 60 drops three times a day. The increase in dosage of

the tincture can be accomplished by adding 5 drops every week until 60 drops is taken three times daily. A tincture of belladonna has also been reported as of value. All these drugs may produce a reaction of overdosage. This is realized by an excessive dryness of the mouth, dilatation of the pupils and its associated decrease of visual accommodation and a mild delirium. When this occurs the patient should be taken off the medication for a time or the dose must be decreased. The patient should not be excited and should be in as quiet surroundings as is possible. Strenuous kinds of entertainment should be discouraged. Otherwise he should lead an active life and work if possible. Cold water treatments, exercises, sun baths, vigorous massage and faradization are all contraindicated. Vitamin B₆ has been reported favorably by some investigators.

ERUPTION OF INFANTS' TEETH, FEVER AND LANCING

To the Editor:—In the town I am practicing in it seems to be the rule to "lance babies' teeth" for all fevers and other disturbances that may bother the infant. In all the pediatrics I have had I cannot recall this teaching. As a matter of fact, recollection causes me to believe that it is a technic held in disrepute. I wish to get expert opinion on this subject to satisfy my lack of knowledge on it.

Alex J. Otten, M.D., McCloud, Calif.

ANSWER.—In years past the practice of lancing the mucous membrane over erupting teeth of infants or rubbing the teeth through with a smooth hard surface object was far more common than present opinion believes warranted. Yet there are times when the procedure may be used to advantage.

Rarely if ever can the cutting of a tooth be considered a direct cause of fever. The discomfort may make a fretful baby. This in turn may interfere with both rest and feeding, which may lower resistance and predispose infection. Increased salivation during teething may affect digestion.

It sometimes happens that the soft tissue of the mucous membrane offers greater than usual resistance to the erupting tooth. In such instances the prolonged period of irritation may indirectly contribute to fever or digestive disturbances. Under circumstances of this sort either lancing the gum or rubbing the tooth through is justified and in these occasional instances will be found to contribute materially to the comfort of the baby and the consequent peace of mind of the entire household.

TOXICITY OF STODDARD SOLVENT

To the Editor:—A patient working in a locomotive repair shop complains of pains in the arms and hands and irritation of the eyes. The symptoms complained of indicate a neuritis. He has been using a preparation called Stoddard solvent, made by the Waverly Oil Company, and is under the impression that this compound is responsible for the symptoms. Any information that you can give me as to the toxicity at this material will be appreciated.

J. P. Hobson, M.D., Springboro, Pa.

ANSWER.—Stoddard solvent is a petroleum distillate having a flash point of not less than 100 F. Its distillation range is such that not less than 50 per cent is recovered in the container with a thermometer at 350 F. with a distillation end point not higher than 410 F. This solvent thus has such properties that explosions and fire hazards are much lowered over petroleum spirits, which have a flash point of 70 F. This substance was formulated for chief use in the dry cleaning industry, but many other lesser applications have developed, such as for metal cleaning. Owing to its low power of evaporation, this substance is regarded as less toxic than petroleum naphtha, gasoline, petroleum spirits, volatile mineral spirits and the like. Similarly, it is regarded as less of a skin irritant or skin fat solvent, since its boiling range is nearer that of petroleum light lubricating oils. Assuming that evaporation may take place and that damage to exposed workers may arise, the clinical picture is likely to conform to that of petroleum distillates in general. All such substances are reported as capable of producing a typical picture associated with some or all of the following objective observations: Loss of weight, tachycardia, secondary anemia, skin irritation, gastrointestinal irritation, mental depression, muscular twitchings, tremors and the like.

It is believed that the irritation of the eyes mentioned possibly may be attributed to the vapors of Stoddard solvent, but the occurrence of a neuritis with pains in the arms and hands appears improbable. For information on specifications and chemical attributes, reference is made to "Stoddard Solvent," a Department of Commerce Report (Commercial Standard CS3-28), Government Printing Office, Washington, D. C., 1929. For clinical data, see "Poisoning by Petrolatum Distillates," by E. R. Hayhurst, *Industrial Medicine* 5:53 (Feb.) 1936.

INFLAMMATION OF SPHENOIDAL SINUS

To the Editor:—A white woman aged 33, a school teacher, for the past five years has been suffering with severe retrobulbar pain, diplopia, dizziness, pain in the occipital region, dimmed vision (and at times it is blurred) and unsteady gait due to the diplopia during an attack. She is physically well nourished, mentally alert and there is nothing of significance except a papilledema of the right eye persisting for five years and some atrophy of the nerve. All reflexes are present. She has been carefully examined except for an encephalogram and seen by one of our best local neurologists and discharged from the New York Neurological Institute with the diagnosis chronic encephalitis. The past history of this patient is interesting. She had an appendectomy one week after marriage, has no sexual desires, and complained of abdominal pain for six months following the operation. Brain tumor was ruled out. An otolaryngologist made a diagnosis of ethmoiditis. Other impressions were multiple sclerosis. My impression is a neurosis or a vitamin deficiency. I have been seeing the patient for about one month and have been giving her intravenous thiamine hydrochloride from 15,000 to 30,000 units every third day and short wave therapy to the frontal sinuses. She has received much relief and then over this past week end had an acute exacerbation of her syndrome. Could you suggest anything in the way of treatment or diagnosis?

M.D., New York.

ANSWER.—A neurosis will not cause a papilledema or an atrophy of the optic nerve. One sided papilledema and contralateral atrophy are extremely suggestive of the Foster Kennedy syndrome due to inflammation of the sphenoidal sinus. Multiple sclerosis is not probable in the presence of a papilledema but must be ruled out by continued neurologic observation. Vitamin deficiency is pretty much out of the question as an etiologic factor.

In view of lack of specific diagnosis, it is suggested that non-specific, shock-producing foreign protein therapy might be of value.

TETANY AND POSSIBLE SPRUE

To the Editor:—A man with nontropical sprue lost considerable weight and also developed tetany, having had diarrhea for three years. The tetany was not controlled by calcium lactate, and calcium had to be given intravenously daily. However, since switching to calcium chloride the tetany has been under control. His sprue has improved somewhat following liver therapy and low fat diet, and his weight has picked up although he is still far from normal. I have been unable to get vitamin D into him, and he still finds it necessary after a year and a half to take calcium chloride. Have you any suggestions as to how I can (1) get vitamin A and vitamin D into this patient, (2) increase his weight and (3) eliminate the constant taking of calcium? Will he ever be cured of sprue or must he take liver for the rest of his life?

Walter J. Farr, M.D., Teaneck, N. J.

ANSWER.—One would seriously question the diagnosis in this case. Certainly more data are necessary on the entire condition of the patient, including the results of a course of parathyroid extract hypodermically. The thyroid status and basal metabolic rate would need to be known. It would be necessary to determine the acid-base equilibrium of the blood, as tetany may arise either from deficiency of calcium with normal alkalinity or from a normal calcium level with excessive alkalinity. One would like to know whether hyperventilation is present with its attendant increase of alkalinity, in which case one would consider the administration of diluted hydrochloric acid solution or ammonium chloride. If the tetany is due simply to deficiency of vitamin D, the use of a sun lamp or direct sunlight, together with administration of vitamin D, would be indicated. If the tetany is due to deficient quantity or function of parathyroid tissue, it would be necessary to give parathyroid extract. The proper use of parathyroid extract, acids, viosterol in oil, sunlight and calcium salts intravenously covers the therapy in these particulars. X-ray studies of the bones should be made to determine the degree or presence of osteoporosis.

If the fault is with enteric absorption, it would be worth while trying the effect of thyroid extract and purified bile salts combined with a careful diet. This diet should approximate Fairley's ratio of protein 1.0, fat 0.3 and carbohydrate 1.3, with a gradual increase to the formula protein 1.0, fat 0.36, carbohydrate 2.0. Liver extract may be tried in large doses parenterally, 10 cc. in the muscle daily for from twenty to thirty days. Sometimes this can be supplanted or increased by liver extract in powder form by mouth, 4 Gm. three times a day with meals.

With regard to the numbered questions: 1. Vitamin A can be given intramuscularly, in the form of carotene (provitamin A) in aqueous suspension. (A preparation of this kind is marketed by the S. M. A. Corp.). It would seem best to rely on ultraviolet therapy for providing a vitamin D effect.

2. Increase of available fat will follow proper intestinal absorption. The Althausen galactose tolerance curve should be secured in order to estimate the absorptive power from the small intestine.

3. Nontropical sprue is characteristically resistant to treatment, and the prognosis must of necessity be guarded.

BLINDNESS FROM HEMORRHAGE INTO OPTIC
NERVE CANAL

To the Editor:—I should be grateful for any information concerning the etiology of blindness and the prognosis for return of vision in the following case history: The patient was struck over the left temple by a mounted pair of antlers. They fell perhaps 12 inches from the wall. She was momentarily unconscious but subsequently, except for moderate pain, headache and the rapid development of a large ecchymosis about the left orbit, all right. As soon as the excitement incident to the injury subsided (within a few minutes) the patient noticed that she could not see out of the left eye. I saw her for the first time some two weeks after the injury. At examination there was a minor abrasion beneath the left orbit and a large discolored ecchymosis about the left orbit. The temporal side of the left sclera was lightly stained with yellowish (blood) pigment. Ocular movements were normal. The cornea, aqueous, iris and pupil appeared normal. Subjectively the patient was completely blind in the left eye. Objectively there was no reflex to light in the injured eye, nor did the right (normal) eye give a consensual reflex to light shined into the left eye. However, variations in the intensity of light shined into the right (normal) eye resulted in consensual changes in the left (blind) pupil. The left pupil dilated evenly under atropine. Ophthalmoscopically the lens and vitreous were clear. The disk and retina appeared normal, with no creases or folds of the retina. The arteries and veins appeared normal. The nerve head and retina were of normal color (as far as a backwoodsman without special training could tell). Two months after injury there is still no light perception in the left eye and examination is essentially the same except that (1) ecchymosis about the orbit and discoloration of the sclera are cleared and (2) the nerve head is *perhaps pale*. (This last observation is questionable.) No roentgenogram of the orbit has been taken and no treatment prescribed. What additional examination and therapy, if any, should be undertaken?

M.D., Montana.

ANSWER.—The loss of sight was probably due to hemorrhage within the sheaths of the optic nerve, in all likelihood within the optic canal. This may have been due to a fracture of the orbit which could be detected even this late by careful x-ray examination. Immediate pressure by the blood within the nerve sheaths on the fibers of the optic nerve caused the immediate loss of sight. Absorption from this area is slow and consequently the pressure was maintained sufficiently long to cause a pressure atrophy of the nerve fibers. About six weeks is required before such atrophy becomes visible ophthalmoscopically in the form of so-called primary pallor of the disk. Had the condition been diagnosed at once, immediate radical opening of the orbit with drainage windows in the sheaths of the nerve (Elschnig-Mueller operation) might have resulted in complete restoration of vision; but now there is nothing that can be done and there is no possibility of restoring the vision.

REFRIGERATION NOT INDICATED FOR
CHRONIC ALCOHOLISM

To the Editor:—Because I can find no reference at all to the treatment of chronic alcoholism by the new "refrigeration method," I am writing to ask if there is anything at all to it. I am entirely ignorant of its possibilities and feel sure that there is nothing to it. The wife of a chronic alcoholic addict tells me that she has both read in the newspapers and been told of the method being used with success. I wish to feel more secure before discouraging her more completely about it. Any information will be appreciated.

M.D., Connecticut.

ANSWER.—No instance in which refrigeration has been used for chronic alcoholism has been found. Prompt and impressive relief of pain which follows refrigeration has, however, been observed. It has been possible to remove patients from dependence on narcotics following refrigeration and this has led to the observation of the effect of refrigeration and its method on narcotic addiction in a few instances. Refrigeration does not appear to be applicable to the problem concerned with chronic alcoholism, as refrigeration favors cerebral edema, which is an undesirable complication of chronic alcoholism. Its use, therefore, might be expected to be highly detrimental rather than beneficial.

ASPHYXIAL DEATH

To the Editor:—I wish to know the postmortem picture that one would expect to find in a baby about 3 months old that smothered to death lying on its face. Would there be any characteristic blood abnormalities? Can you tell me where I can find the answers to these questions or answer them?

M.D., Indiana.

ANSWER.—In most instances, though not invariably, one would expect to find unusually dark patches of postmortem lividity on the body surfaces, particularly those toward which the blood would normally gravitate. The lips, mucous membranes of the mouth, the nose, ears and finger and toe nails are of a purplish hue. There are no marks of localized violence on the face and neck other than might be expected from the nature of the material on which the body was lying.

Internal organs show uniform congestion and engorgement with dark colored blood. The vascular system is engorged,

particularly the veins and the right side of the heart, which is distended. The left side of the heart is usually contracted. As in all asphyxial deaths, the blood remains fluid longer than usual. There are small subendothelial petechiae found on the serous surfaces of the lungs, heart and other organs.

The blood chemistry is of no significance unless the specimen is taken immediately after death. In that event one would find a definite decrease in carbon dioxide combining power and in the oxygen content of arterial blood. Even in nonasphyxial cases these values diminish at a rapid rate after death has occurred.

COLONIC IRRIGATION

To the Editor:—What is the opinion on the colonic irrigating apparatus now used in some cases of colonic and gastric disturbances? I have seen a demonstration with the colonic irrigator but hesitate to approve it until I receive further discussion on this subject.

Richard A. Nagle, M.D., Chicago.

ANSWER.—It is extremely difficult to determine the field of usefulness, if any, of colonic irrigation. While the role of the small cleansing enema and of the medicated retention enema seems well established, colonic lavage has been outrageously exploited in many quarters. There is little evidence to show that it may benefit diseases of the colon and there is none for the stomach. On the other hand, it may cause harm.

No complicated or costly chromium plated equipment is needed or advised. A simple soft rubber tube and glass jar prove adequate.

Before purchasing equipment the writer is advised to read the authorized report on this subject by Dr. Frank H. Krusen of the Mayo Clinic to the American Medical Association Council on Physical Therapy (THE JOURNAL, Jan. 11, 1936, p. 118).

LEAD HAZARD FROM COMMON CONTACTS

To the Editor:—One of the consumers' groups has come into prominence by charging the presence of lead in dangerous quantities in common contacts. These are notably fumes from automobile exhausts in traffic, and foods, particularly chocolate (including the most reputable American brands), and dried fruits, like prunes. Have you any data as to the accuracy of this information?

M.D., Moine.

ANSWER.—It is difficult to answer this query because no mention is made of amounts of lead. Food and Drug officials have set a standard for the amount of lead allowed in foods and have been active in enforcing this requirement. This so-called tolerance is safe, since lead taken in by mouth is much less hazardous than when inhaled as fumes or dust. In the analysis of bones, Barth (*Virchows Arch. f. path. Anat.* 281:146, 1931) found little evidence of accumulation of lead in bones during life. This is the crux of the problem, for if lead is not ingested in sufficient quantity to be stored in bone it is highly unlikely to produce poisoning. The same thing may be said of automobile exhausts in traffic. When lead was first introduced into gasoline there was considerable discussion as to whether many people would not get lead intoxication. No cases of lead poisoning among the general public from this source have developed, so far as known, even in large cities. Some lead may appear in foods which are packaged in lead foil, but tin or aluminum foil is more generally used.

DERMATITIS FROM FORMALDEHYDE

To the Editor:—A patient has been doing comparative anatomy and thereby handling formaldehyde daily for a period of five and one-half months. About two or three months ago she contracted and has continued to have vesicular dermatitis at the hands and edema of both legs. The swelling in the legs goes down at night. An examination reveals no tumor growth. Her blood and urine are normal. She is apparently perfectly well. I know that formaldehyde can provoke arterial necrosis. Could it be a cause at the edema in her legs? It is not Milroy's disease.

William J. MacDonald, M.D., Boston.

ANSWER.—The vesicular dermatitis of the hands of this patient may be caused by the formaldehyde which she handles. Formaldehyde, when used for long periods in concentrations of from 2 to 10 per cent, can set up eczematous lesions of the skin characterized by vesicles and ulcerations. More concentrated solutions may actually cause burns and necrosis of the skin.

The edema of the patient's legs is not caused by exposure to formaldehyde. Nowhere in the literature can there be found such an effect of long exposure to formaldehyde. Irritation of the skin, of the nails and of the mucous membranes of the respiratory tract and of the conjunctivas are the principal toxic effects of exposure to formaldehyde. In rare cases there may occur irritation of the gastrointestinal tract accompanied by

nervous excitement. The fact that the urine is normal indicates that the kidneys are not being irritated.

The edema of the legs may be due to cardiac disease unrelated to exposure to formaldehyde or to mechanical constriction, such as garters, or to accumulated fecal matter pressing on the large veins of the pelvis, or even to a retroverted uterus acting in the same way.

If the dermatitis is due to formaldehyde, the application of a soothing ointment or lotion, and the wearing of rubber gloves while working so as to prevent further contact with the chemical, will relieve the condition.

ESCHAROTIC PASTES AND CANCER

To the Editor:—A patient was treated elsewhere for carcinoma of the lower lip by the application of a paste. She was in severe pain and after some inquiry I found that the paste consisted of zinc chloride, sanguinaria and wheat flour, each in equal parts. Three questions arose in my mind concerning this treatment. 1. Is this approximately the same formula that is used in many of the so-called cancer sanatoriums? 2. Is the efficiency of it enough to warrant its use in any case whatever? 3. What are the dangers and complications which might arise from the use of such treatment? E. E. Gamet, M.D., Lamoni, Iowa.

ANSWER.—1. Zinc chloride is the essential constituent of most of the pastes used in "cancer sanatoriums." The other ingredients undoubtedly vary.

2. Escharotic paste is not indicated in the treatment of any form of cancer. Surgery, radium and x-rays are the accepted methods for the treatment of these lesions.

3. One of the main difficulties connected with the escharotic treatment of cancer lies in the inability to control the treatment. If too little is used, the local or primary growth may not be entirely removed. A second and more important difficulty is the inability to treat the regional lymph nodes.

DYSTROPHIA OF CORNEA

To the Editor:—I should like to have some information concerning a peculiar corneal lesion. A woman about 55 years old has normal vision and does not remember even a minor injury. She states that about one year ago she noticed a yellowish white speck on the cornea, about 4 mm. central to the limbus. No treatment was instituted. During the past month or two the mass has enlarged a little, so that now it resembles a 1 by 2 mm. yellowish white, elevated and umbilical lesion. The edges are sharply defined and there appears a faint infiltration in the substantia propria of the cornea. I should like to have your comments on the diagnosis and suggested treatment. M.D., Michigan.

ANSWER.—It is difficult to give a specific answer as to what type of lesion is affecting the cornea without actually seeing the eye and watching the progress of the condition. The lesion might be included in any one of the many types of dystrophias of the cornea of which little is known as to cause or treatment. A neurogenic basis might also be considered. In addition it is possible that an unknown injury might have caused an infection to occur in the cornea. A test of the corneal sensitivity might give a lead as to the etiologic factor. Another source which must be thought of is a lesion due to yeast, molds and the like. Closely related to the dystrophias of the cornea are such types of degenerations of the cornea and this must also be considered. Treatment in any case must necessarily be guided by the causative factor; however, the prognosis is not good.

ABDOMINAL PAIN AFTER NEPHRECTOMY

To the Editor:—Three years ago I removed a badly infected and enlarged right kidney from a white woman aged 23. Until the past three months she has been enjoying excellent health. Now she has attacks of severe sudden pain in the lower right quadrant of the abdomen requiring morphine for relief. A pelvic examination is essentially negative, as is a urine analysis. On cystoscopy there is nothing abnormal found. I am able to pass a No. 7 urethral catheter up 20 cm. on the right side. At the time of operation I was able to get only a strip of ureter out with the kidney, for the patient's condition was bad. I now ask is her pain due to spasm of the remaining piece of ureter on the right side? What should be done in this case? Should the right ureteral orifice be destroyed by the electric current? M.D., Ohio.

ANSWER.—The ureter remaining following nephrectomy is seldom the cause of abdominal pain. In the rare case in which it occurs, the pain is caused either by stone in the lower end of the ureter or by reflux of urine from the bladder, the ureter acting as a diverticulum.

A plain roentgenogram, and the fact that it is possible to pass a No. 7 catheter to a distance of 20 cm. in the remaining portion of the ureter, should exclude the possibility of stone. A ureterogram would show a dilated ureter if reflux of urine from the bladder is sufficient to cause pain.

In all probability the pain is of extra-ureteral origin.

NASAL VAPOR IN WARM AIR

To the Editor:—A man aged 24 and apparently in good health (except for heavy brown furring or coating of tongue, especially in the midportion and toward the posterior part) complained that he and his mother noticed "a sniffing of a vapor from his nose which looked just like condensed moisture in breath only the atmosphere was not cold at the time." This has happened four times in two years. By repeated exhalations through the nostrils this vapor appeared. It has occurred on arising and also two occasions after eating breakfast. Can you suggest any cause for such a phenomenon? I feel that scientific importance cannot be attached to it. M.D., Kentucky.

ANSWER.—The phenomenon described is indeed strange. There might be several explanations for the condition; each would probably be on a physical basis. There is no reason why it should be a sign connected with a disease process or some physiologic change.

Although it was not cold at the time when the vapor was seen, the patient may have been sitting in the rays of direct sunlight, which would accentuate the moisture in the exhaled air. The nasal passages should be carefully examined to see whether a spur or a peculiarly shaped turbinate has not been the cause of vapor formation when the exhaled air passed over its moist surface. Nasal instillations of oil could also be vaporized in the same way.

The brown coating of the tongue would not seem to be connected with this condition.

DANGER FROM RABIES IN DEAD ANIMALS

To the Editor:—Is there any possibility of infection with rabies from touching any tissues from a dead rabid animal which may be about the streets? If there is that danger, for what period of time from the death of the animal will the virus live under ordinary city street conditions? Murray Greenwald, M.D., Brooklyn.

ANSWER.—So far as known it would not be possible for the infection in rabies to pass through the healthy human skin on touching a dead rabid animal. The possibility of infection through abrasions and wounds of the skin cannot be denied. No definite statement can be made as to how long the virus of rabies can live in a dead animal under ordinary city street or other conditions.

BIRTH PARALYSIS AND WHEAT GERM OIL

To the Editor:—A little boy has spastic paralysis due to a possible birth injury. Please advise the technic and virtues of germ wheat oil treatment. M.D., Florida.

ANSWER.—The wheat germ oil treatment has been suggested only for cases of muscular dystrophy and of amyotrophic lateral sclerosis presumably due to deficiency of vitamin E. Even in these conditions its value is questionable. It would certainly not be effective against the results of birth injuries.

LIMESTONE DUST AND PNEUMOCONIOSIS

To the Editor:—Would you please give me some information regarding a case of pneumoconiosis caused from the inhalation of dust that does not contain silicates but is caused from limestone gravel dust, which has persisted for more than two years without much evidence of improvement. What would be the chances for an ultimate recovery? J. O. McKenney, M.D., Beaver Dam, Ky.

ANSWER.—Relatively pure limestone dust does not produce serious reactions in the lungs, as indicated by the observations in large numbers of cement plant employees. The statement that a pneumoconiosis from this source "has persisted for more than two years without much evidence of improvement" needs amplification. If there are changes of significant nature, they must have been produced by some other cause. If the manifestation of these changes is limited to exaggeration of the normal pulmonary markings in a chest roentgenogram, such changes will probably persist; but they are of little or no clinical significance.

POSTURAL HYPOTENSION

To the Editor:—In *Queries and Minor Notes* for June 15, 1940, page 2404, there appeared an inquiry from a physician concerning a patient whose chief complaints were extreme weakness and dizziness on assuming the upright posture. The description fits in well with the diagnosis of postural or orthostatic hypotension, a symptom complex first described by Bradbury and Eggleston (*Am. Heart J.* 1:73 [Oct.] 1925); since then a number of cases have been reported and it has come to be a well defined clinical syndrome. The characteristic feature of orthostatic hypotension is the marked fall in the systolic and diastolic blood pressures on assumption of the sitting or standing posture. The diagnosis is easily confirmed by blood pressure readings in the prone and erect positions.

J. W. Welty, M.D., Philadelphia.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, July 27, page 323.

BOARDS OF MEDICAL EXAMINERS

ALASKA: Juneau, Sept. 3. Sec., Dr. W. W. Council, Box 561, Juneau.

ARKANSAS: Regular. Little Rock, Nov. 7-8. Sec., Dr. D. L. Owens, Harrison, *Electric*. Little Rock, Nov. 7. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), San Francisco, Oct. 2. *Written examination*. Sacramento, Oct. 21-24. Sec., Dr. Charles B. Pinkham, 1020 N. St., Sacramento.

DISTRICT OF COLUMBIA, Washington, Nov. 11-12. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Tampa, Nov. 18-19. Sec., Dr. W. M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, Oct. 8-9. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, Oct. 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Oct. 1-3. Superintendent of Registration, Mr. Lucien A. File, Springfield.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, Dec. 3-5. Sec., State Board of Health, Dr. A. T. McCormack, 620 Third St., Louisville.

MARYLAND: *Medical*. Baltimore, Dec. 10-13. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homoeopathic*. Baltimore, Dec. 10-11. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: Lansing, Oct. 9-11. Sec., Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: Minneapolis, Oct. 15-17. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity*. Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: *Reciprocity*. Helena, Sept. 30. *Written*. Helena, Oct. 1-2. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: *Reciprocity with oral examination*. Aug. 5. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW JERSEY: Trenton, Oct. 15-16. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 7-8. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Sept. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Building, Albany.

OKLAHOMA: Oklahoma City, Dec. 11. Sec., Dr. James D. Osborn Jr., Frederick.

PUERTO RICO: San Juan, Sept. 3. Sec., Dr. O. Costa Mandry, Box 3854, Santurce.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 4-6. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WEST VIRGINIA: Morgantown, Oct. 31-Nov. 2. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: Madison, Jan. 14-17. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, October. Sec., Dr. M. C. Keith, Capitol Building, Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, Sept. 17. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

CONNECTICUT: New Haven, Oct. 12. Chairman, State Board of Healing Arts, Dr. Charles M. Bakewell, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, Oct. 21-22. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Gainesville, Nov. 1. Applications must be on file not later than Sept. 16. Sec., Dr. John F. Conn, John B. Stetson University, De Land.

MINNESOTA: Minneapolis, Oct. 1-2. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: Lincoln, Oct. 1-2. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, Oct. 26. Sec., Mr. Charles D. Bryne, State Board of Higher Education, University of Oregon, Eugene.

SOUTH DAKOTA: *Examination*. Yankton, Dec. 6-7. *Endorsement*. Dec. 21. Sec., Dr. Gregg M. Evans, Yankton.

WISCONSIN: Madison, Sept. 21. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee.

Montana April Report

Dr. S. A. Cooney, secretary, Montana State Board of Medical Examiners, reports the written examination held at Helena, April 2-3, 1940. The examination covered ten subjects. An average of 75 per cent was required to pass. Five candidates were examined, all of whom passed. Eight physicians were licensed by reciprocity and one physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Loyola University School of Medicine.....	(1940)*		81.1
Northwestern University Medical School.....	(1936) 83.4,	(1940)†	76.6
Rush Medical College.....	(1939)		81.7
University of Minnesota Medical School.....	(1940)‡		83.8

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of California Medical School.....	(1936)		California
Rush Medical College.....	(1938)		Colorado
University of Minnesota Medical School.....	(1939)		Minnesota
St. Louis University School of Medicine.....	(1938)		Missouri
University of Nebraska College of Medicine.....	(1938)		Nebraska
Queen's University Faculty of Medicine.....	(1927)		Michigan

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists.....	(1938)		N. B. M. Ex.

* This applicant has completed four years' medical work and will receive the M.D. degree on completion of internship. License has not been issued.

† This applicant has received the M.B. degree and will receive the M.D. degree on completion of internship. License has not been issued.

‡ License has not been issued.

Arizona April Report

Dr. J. H. Patterson, secretary, Arizona State Board of Medical Examiners, reports the written examination held at Phoenix, April 3-4, 1940. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Four candidates were examined, all of whom passed. Five physicians were licensed by reciprocity and one physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1920)		85.8
Loyola University School of Medicine.....	(1939)		90.6
Harvard Medical School.....	(1938)		80.7
Columbia University College of Physicians and Surgeons.....	(1929)		79.1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Northwestern University Medical School.....	(1927)		California
University of Minnesota Medical School.....	(1938)		Minnesota
Washington University School of Medicine.....	(1936)		Missouri
University of Tennessee College of Medicine.....	(1935)		Tennessee
Baylor University College of Medicine.....	(1936)		Texas

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists.....	(1938)		N. B. M. Ex.

District of Columbia May Report

Mr. Paul Foley, assistant secretary, District of Columbia Board of Examiners in Medicine and Osteopathy, reports the written examination held at Washington, May 13-14, 1940. The examination covered nine subjects and included sixty questions. An average of 75 per cent was required to pass. Thirty-two candidates were examined, thirty of whom passed and two failed. Ten physicians were licensed by reciprocity and ten physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1939)		82*
George Washington University School of Medicine.....	(1938)		78.6*
82.8, 84.5, 84.8, 88.8,* (1939) 81,* 81.3,* 81.5,* 84.3,* 84.5,* 85.8,* 86.1,* 86.6,* 86.8,* 87.6,* 88.1,*			
Georgetown University School of Medicine.....	(1934)		80.6,
(1937) 82.5, 83.3, (1938) 84.6,* (1939) 85.1*			
Rush Medical College.....	(1936)		75.1
Tufts College Medical School.....	(1935)		84
New York University College of Medicine.....	(1935)		83.1
Jefferson Medical College.....	(1939)		85.6*
University of Penns.....	(1938)		85.8
University of Virgin.....	(1939)		78.5*
Queen's University.....	(1936)		84.5
University of Toront.....	(1928)		80.1

School	FAILED	Year Grad.	Number Failed
George Washington University School of Medicine.....	(1935)		1
Howard University College of Medicine.....	(1937)		1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Georgetown University School of Medicine.....	(1934)		W. Virginia
Indiana University School of Medicine.....	(1932)		Indiana
University of Louisville School of Medicine.....	(1937)		Kentucky
Johns Hopkins University School of Medicine.....	(1935)		Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1936), (1937)		Maryland
Medical College of the State of South Carolina.....	(1911)		S. Carolina
University of Tennessee College of Medicine.....	(1930)		Maryland
University of Virginia Department of Medicine.....	(1935)		Virginia
Queen's University Faculty of Medicine.....	(1928)		Wisconsin

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
George Washington University School of Medicine.....	(1937, 2), (1938, 2)		N. B. M. Ex.
Georgetown University School of Medicine.....	(1935), (1937, 2)		N. B. M. Ex.
Tufts College Medical School.....	(1936)		N. B. M. Ex.
University of Rochester School of Medicine.....	(1934)		N. B. M. Ex.
University of Oregon Medical School.....	(1933)		N. B. M. Ex.

* License has not been issued.

Book Notices

Handbook of the Hospital Corps United States Navy 1939. Published by the Bureau of Medicine and Surgery under the authority of the Secretary of the Navy. Cloth. Price, \$1.75. Pp. 1,015, with 201 illustrations. Washington, D. C.: Supt of Doc., Government Printing Office, 1939.

The last previous edition of this book was published in 1930. Unfortunately, even the present edition is not quite up to date, since the 1935 edition of New and Nonofficial Remedies served as its basis for drugs not included in the Pharmacopeia or in the National Formulary. Planned essentially as a medical guide for the hospital corpsmen of the Navy Medical Department, the work approximates a household medical work, with chapters on minor surgery and first aid, emergency dental treatment, nursing, hygiene, allergy, the venereal diseases, field sanitation, diets, pharmacy, chemistry, the control of hospitals and many other suggestions. There is valuable information on the use of x-rays, on laboratory procedures and technic, on chemical warfare and on medicolegal problems. Certainly the book must be exceedingly useful, particularly to those members of the Navy Service who are not in immediate contact with medical officers.

Handbuch der Virusforschung. Herausgegeben von Prof. Dr. R. Doerr und Prof. Dr. C. Hallauer. Zweite Hälfte: Die Virusarten als Infektions Agenzien—Die Immunität gegen Virusinfektionen—Die Technik der experimentellen Erforschung phytopathogener Virusarten. Bearbeitet von J. Craigie et al. Paper. Price, 96 marks. Pp. 547-1384, with 19 illustrations. Vienna: Julius Springer, 1939.

The second half of this encyclopedic and critical review of the present state of knowledge in this rapidly advancing field of human and comparative medical science is devoted to three major fields, to wit the viruses as agents of infection, immunity against such infections, and the technic of investigation of plant viruses. Dr. Doerr surveys the natural transfers of viruses by germinative, intra-uterine, contact methods and arthropod vectors and the experimental ones by intracerebral, intraneural, intranasal and corneal inoculation and culture on the chorio-allantois of the chick embryo. He also reviews the qualitative analysis of viruses by serial passage, determination of specificities, detection of unsuspected latent infections, the establishment of genetic relationships among viruses, the etiologic associations of virus + bacteria and virus + virus, and methods of identification of viruses. The quantitative study of viruses is carried on by titration and the count of colonies of bacteriophage, lesions on the chorio-allantois, pox on skin and cornea, and lesions on leaves of plants. The significance of the results is tested by mathematical analysis.

A chapter of prime medical interest is that devoted to the spread of the virus in the body of the host. It may localize at the port of entry, enter and remain in the blood, infect an organ distant from the port, spread from the port in blood, lymph or nerve, and exhibit affinities to and interrelations with the circulatory and neurotropic paths. The experimental, pathologic and clinical consequences of virus invasion are reviewed in the light of evidences from the study of herpes and poliomyelitis, the spread within the central nervous system and the centrifugal transport from the central nervous system.

Dr. Doerr also reviews the tropisms and specific localizations of viruses discussing the as yet unsolved problems arising from the invasion of the host by nonmotile infectious agents and the theories proposed to explain it, such as germ layer affinity, tissue tropisms, neurotropism and pantropism, and the significance of variability in localization.

Dr. G. M. Findlay of the Wellcome Research Bureau of London reviews variations in viruses, noting that, although there is no clear evidence that hereditary characteristics in viruses are transmitted by structures of the type of genes, much less of chromosomes, there is no essential difference to be found between variations in viruses and those in unicellular and multicellular organisms. These variations are in virulences, types of tissue lesions in the host, antigenic character, lesion and antigenic character, and chemical and physical properties of the virus proteins. There is some evidence of the origin of new diseases within historical times, such as St. Louis encephalitis. Limitation to small geographic area suggests recent origin. Origina-

tion of variants in virus has been observed in the same tissue in the same host species, in the tissue but in different species, in a different tissue of the same and different species of host, after prolonged growth in tissue culture, and following physical changes in environment such as exposure to glycerin and high temperatures. The change in environment may conceivably act by environmental change modifying dominance, by abrupt mutations of genetic character, by selection from an already heterogeneous assemblage of viruses, or by the induction of temporary but reversible modifications. The possibility of such changes should be greater among viruses than among animals and plants because of their higher rate of propagation. This reduction of the time factor in viruses favors the study of evolution in them as over against its study in longer lived plants and animals.

Dr. O. Thomsen of Copenhagen reviews the rapidly growing literature on viruses as tumor-inducing agents. He expresses a doubt that they constitute a specialized unified group, since they appear to grade on the one hand into merely cell proliferating types and on the other into those inducing pathologic and degenerative processes.

Dr. James Craigie reviews the antigen functions of viruses and the serologic reactions of viruses in vitro, and Dr. C. Hallauer and F. Magrassi discuss acquired immunity against virus infections.

Mr. Kenneth M. Smith of the Virus Research Station of the School of Agriculture at Cambridge, England, discusses the principles of plant virus research, a field offering unique opportunities for the study of viruses not available with animal viruses. The most spectacular achievement in this field was the isolation of a virus protein of heavy molecular weight having all the properties of the virus itself. The identity of the two is suggested but not as yet satisfactorily demonstrated. The use of graded colloidal membranes in ultrafiltration has made possible the determination of the sizes of the particles of the various viruses. The concentration of virus particles and their aggregation have been determined by the statistical analysis of the numbers of local lesions produced on leaves of susceptible plants by inoculation. The study of the viruses in their insect vectors has as yet given no evidence of their multiplication in the body of the insect, though an animal virus in the mosquito has been found to multiply in it. The serologic reactions of plant viruses serve to identify them and to reveal unsuspected relationships. The existence of virus strains, cross immunities and attenuation of virulence by heat leads to hope of finding a vaccine against some plant viruses and of facilitating the breeding of resistant stocks of plants.

The book closes with a tabular presentation of all known plant and animal viruses. The two volumes reveal the complexities, great biologic and medical significances and undoubted promise of virus research.

The Management of Obstetric Difficulties. By Paul Titus, M.D., Obstetrician and Gynecologist to The St. Margaret Memorial Hospital, Pittsburgh. Second edition. Cloth. Price, \$10. Pp. 968, with 373 illustrations. St. Louis: C. V. Mosby Company, 1940.

It seems odd that a book devoted exclusively to obstetric difficulties should occupy as many pages as most standard textbooks of obstetrics, which contain both normal and abnormal obstetrics. Yet a careful study of this book reveals that Titus has closely adhered to his theme. One may question only whether the subject of sterility, which occupies seventy-seven pages, and the treatment of the cervix by electrical apparatus in the nonpregnant woman properly belong in a book on obstetric difficulties. The author himself is aware of this question, because in the preface he says "Obstetrics and gynecology interlock so closely that there is ample reason for including chapters on pelvic floor damage, postpartum uterine misplacements and their treatment, tumor growths complicating pregnancy, ectopic pregnancy, electrovaginal coagulation and conization for postpartum cervicitis, as well as sterility and its treatment." The book is based on the author's extensive experience both as a clinician and as a teacher. However, throughout the book he gives credit to many of his confrères and particularly to J. Whitridge Williams, his former chief. He exhibits a conservative attitude in almost all branches of obstetrics and his advice is in accord with the best obstetric judgment. The book is written in an easily

readable style, which will appeal to students and general practitioners. The illustrations are unsurpassable and greatly enhance the value of the book. Titus has considerably improved his book in the second edition by including information about all the recent advances in the diagnosis and treatment of obstetric difficulties. He is to be congratulated on having accomplished his aim so admirably.

Studies on Pain Conduction in the Trigeminal Nerve: A Contribution to the Surgical Treatment of Facial Pain. By Olof Sjöqvist. Acta psychiatrica et neurologica Supplementum XVII. Paper. Price, \$3. Pp. 139, with 38 illustrations. New York: G. E. Stechert & Co.; Helsingfors: Mercators Tryckeri, 1938.

The hope entertained in Sjöqvist's interesting treatise is that in the treatment of trigeminal neuralgia a differential section of a bundle of pain fibers in the medulla can abolish pain and preserve other sensations to the face, particularly the sense of touch. He has operated on nine patients by means of this intriguing procedure with interesting results and without deaths. That sensations carried by the trigeminal nerve become segregated in the sensory root has been demonstrated by partial sections of the sensory root at the pons. That they then are carried by different tracts in the brainstem would appear to be assured. Spiller long ago advanced such a view. Sjöqvist attempts to utilize this fact by cutting only the pain fibers in the medulla. At least, he appears to have identified this tract with sufficient accuracy to be able to spare the tactile sensation to the face after division of this tract by operation. The thermal fibers appear, however, to be so closely allied with the pain fibers that they too are lost, but on the whole the sensation of touch is quite well preserved. The burden of proof is, of course, on the introduction of a new operative attack on trigeminal neuralgia. There are now two excellent procedures which give almost perfect results. The technical side of Sjöqvist's procedure is certainly not easier than either of the two other attacks, the temporal and suboccipital. Nor is it clear that there are any improved results for partial section of the sensory root that will abolish pain by cutting pain fibers only and with little or no loss of other types of sensation. In three of his nine cases paralysis of the vocal cord has followed the operation, owing to the contiguity of these fiber tracts. In two of his cases benefit did not result and section of the sensory root was necessary subsequently. Sjöqvist is more than fair and strikingly objective in his presentation and makes no claims for its superiority over the present approved methods. It is indeed a beautifully conceived and interesting point of attack based on highly scientific anatomic and physiologic studies. Its acceptance or rejection can be determined only with time, when its assets and liabilities are better defined. One may well doubt its value and fear the attack on the medullary contents with such concentrated important functioning tracts lying so closely adjacent. If something goes wrong, serious consequences may ensue. However, only time can evaluate any new procedure and his anticipations and fears may prove to be groundless.

Anatomie générale: Origines des formes et des structures anatomiques. Par H. Rouvière, professeur d'anatomie à la Faculté de médecine de Paris. Paper. Price, 70 francs. Pp. 192, with 96 illustrations. Paris: Masson & Cie, 1939.

Rouvière is already well known in this country through his books and papers, especially his *Anatomie humaine descriptive et topographique* and through his *Anatomie des lymphatiques de l'homme*. The present volume is the result of a thoughtful and thorough study of the physical and chemical and biologic factors which influence the growth and the structure of bones, cartilage, ligaments, circulatory apparatus, muscles and tendons, lungs, liver and kidneys. This study lies in the field intermediate between biology and physics where many think biologic science is likely to make most progress in the next few decades. Undoubtedly processes that are frankly physical or chemical play a large part in animal bodies, but always they are combined with biologic processes; it is better understanding of this combination that is needed. Biologic processes consist partly in ontogenic stimuli acting throughout life and in their interaction with environmental stimuli. The relation of the germ cells with the rest of the body is a matter of first importance in such studies. Rouvière has a definite and interesting idea of this

relation, expressed with characteristic French clearness in the introduction. All parts of the body, even the most minute, are connected with the germ plasm by the blood stream; hormones and specific substances are carried from body cells to germ plasm. Changes in these parts may conceivably influence germ plasm. The latter contains dominant and recessive elements. Somatic influences may change the recessive to dominant. He finds this change more often in the mesenchyme than in the definite germ layers (ectoderm, mesoderm, endoderm); therefore it is best looked for in bones, cartilages, tendons and circulatory organs, that is in the structures which are especially considered in this book. The idea and the thorough study of these structures in relation to it make this book interesting and thought provoking for every one interested in the fundamental principles of morphology.

First Aids in Reading Difficulties. By S. Weir Newmayer, A.B., M.D. Cloth. Price, \$2. Pp. 162, with illustrations. Philadelphia: North American Printing Company, 1940.

The foundation of education is reading. It is therefore desirable to develop speed in reading, to maintain respect and love for the art and science of reading, to encourage good reading and to discourage bad or wasteful reading. The author is convinced that children are ready to read in the first grade when considered from the development of the physiology of the visual organs, but of course reading involves not only seeing the words but also understanding them and interpreting them. Extensive tests have been made on children from the point of view of their ability to read so far as concerns particularly the eye. Special glasses are needed for visually handicapped children. There must be training of the eye, the provision of suitable glasses and attention to the hygiene of the eye to make certain that the child is not hampered in his education by difficulty with vision. The author provides a series of discussions covering lighting and vision which will aid children in learning to read.

The First Five Years of Life: A Guide to the Study of the Preschool Child from the Yale Clinic of Child Development. By Arnold Gesell, M.D., and Henry M. Halverson, Ph.D., Helen Thompson, Ph.D., Frances L. Hig, M.D., Burton M. Castner, Ph.D., Louise Bates Ames, Ph.D., Catherine S. Amatruda, M.D. Cloth. Price, \$3.50. Pp. 393, with illustrations. New York & London: Harper & Brothers Publishers, 1940.

The studies of Dr. Arnold Gesell and his associates on babies have been widely discussed in many important general periodicals. This study has been going on for some fifteen years, sponsored by the National Research Council and similar organizations. Some of the previous volumes have discussed psychologic development from birth to the sixth year, the psychology of early growth and similar subjects. The present volume traces carefully the growth of the child from 1 to 5, discussing his abilities at various ages. The book is fully illustrated with photographs taken from motion pictures, which provide definite evidence of steps in the motor progress of the child. Other chapters concern language development, personal-social behavior, adaptations to peculiar conditions and studies of individuality. There is also a complete presentation of the records used, a bibliography and an index. The work of the Yale Clinic of Child Development is recognized as standard in this field. It will be of immense interest to all of those concerned in the study and training of children and is obviously invaluable particularly to the pediatrician, who must have far more than an ordinary knowledge of child psychology.

Pneumoconiosis (Silicosis): The Story of Dusty Lungs. A Preliminary Report. By Lewis Gregory Cole, M.D., Director of Silicotic Research, John B. Pierce Foundation, New York City, and William Gregory Cole, M.D. Cloth. Price, \$1. Pp. 52, with appendix with illustrations. New York: John B. Pierce Foundation, 1940.

The authors state that this booklet was written free from the bias of writers who are familiar with the literature. Professing to have this unfamiliarity, they then promptly belie their statement with intimate descriptions of work of others and pay tribute to the past teachings of many, particularly in the roentgenology of silicosis. The book claims to present revolutionary and novel ideas. The only novelty discovered was the introduction of inept lay terms to take the place of technical nomenclature which has stood up well and has been understood by technical persons, including the authors. In order to study and to understand the metabolism of inhaled

silica particles, phagocytosis and fibrosis, it is not necessary to be led "on a travelogue of dust flecks." The naive omission of the proved etiology and mineralogy of silicosis, covered so adequately by Gardner, and the total ignoring of the role of tuberculosis in the silicosis problem detract greatly from the report. The authors would seem to have been badly mixed on the use of dark field microscopy vs. polarized light, which are bandied about as 'being more' or less 'synonymous.' The appendixes consist of two of the authors' reprints, one on the roentgenologic diagnosis of silicosis (*Radiology* 33:261 [Sept.] 1939) and the other on the dyspnea of silicosis (*THE JOURNAL*, Sept. 23, 1939, p. 1216).

Textbook of Healthful Living. By Harold S. Diehl, M.A., M.D., Sc.D., Professor of Preventive Medicine and Public Health, and Dean of the Medical Sciences, University of Minnesota, Minneapolis. Second edition. Cloth. Price, \$2.50. Pp. 634, with 63 illustrations. New York & London: McGraw-Hill Book Company, Inc., 1939.

First published as a popular work in hygiene, this volume has now become a textbook used in many schools and colleges. The present edition is especially revised for that purpose. There are new chapters on modern parenthood, community health and organized health work. Some of the sections of the original book have been omitted as not having special interest for the student in hygiene. A number of appendixes to the volume provide tables of standard weights, nutritional values of foods, data on the control of communicable diseases, and especially a personal health record so that every student may fill this out for himself and thereby receive more information as to the factors that are important to personal health and hygiene than in any other way. The great success of this volume is an indication of its usefulness.

Trapping the Common Cold. By George Sanford Foster, M.D. Cloth. Price, \$1.25. Pp. 125. New York, London & Edinburgh: Fleming H. Revell Company, 1940.

This book sets forth the author's ideas of how to avoid the common cold. Some of the advice with respect to sleep, diet, exercise and the avoidance of infection is excellent, but it is mixed with unscientific material such as the advice to use raw milk, the insistence on a special posture during sleep, over-emphasis on exercise, cold bathing and posture and, above all, the unqualified promise with respect to the common cold that its prevention "is easy and the knowledge of means ready at hand." The text is repetitious and not well organized. In mentioning the infectious agents involved in the common cold, the filtrable virus is omitted. The dietary advice is sketchy and inadequate.

Beiträge zur Physiologie und Klinik der weiblichen Genitalorgane im Kindesalter. Von Priv. Doz. Dr. László v. Dobszay. Mit einem Vorwort von Prof. Dr. Jenő Kramár, Direktor der Universitätskinderklinik in Szeged. Acta litterarum ac scientiarum Reg. Universitatis Hung. Francisco-Josephinae, Sectio medicorum, Tom. VIII, Fasc. 3. Redigunt: J. Baló, D. Miskolczy et St. Ruzsnyák. (Acta med. Szeged). Paper. Price, 7 marks. Pp. 152, with 7 illustrations. Budapest: Egenbergersche Buchhandlung Karl Rényi; Leipzig: Johann Ambrosius Barth, 1939.

This book, which deals with the physiology and pathology of the female reproductive organs of children, should be of interest to gynecologists, pediatricians, dermatologists and those interested in venereal diseases. It is generally assumed that the internal genitalia of female children lie dormant during childhood and hence cannot give rise to any disturbances. This is not true. Recent advances in endocrinology, for example, have demonstrated that activity does occur in these organs, particularly shortly after birth and at puberty. The author has devoted eight years of investigation to this study of the female reproductive organs in young girls and he has reviewed the literature on this subject. The book is divided into two parts, one of which deals with the physiology of the genital organs in female children and the other with pathologic conditions in these organs. In the first section the author first describes the anatomy of the genitalia and then he takes up the physiologic phenomena which appear in the newborn and in girls at puberty. In the second section the author considers gonorrheal infections and nongonorrheal infections in young girls. At the end of the book is an extensive bibliography. This is an excellent reference book for all who are interested in the medical aspects of female children.

The Medical Annual: A Year Book of Treatment and Practitioner's Index. Edited by H. Lethby Tidy, M.A., M.D., F.R.C.P., and A. Rendle Short, M.D., B.Sc. Fifty-Eighth Year 1940. Cloth. Price, 20s. Pp. 604, with 127 illustrations. Bristol: John Wright & Sons Ltd., 1940.

Featured in the Medical Annual for 1940 is material on the sulfonamides, flying, the vitamins and the treatment of war injuries. This excellent review of the medical literature of the year is now in its fifty-eighth annual volume, indicating obviously that it serves a useful purpose. The British contributors are persons of note who have had extensive experience in the fields for which they are responsible. This volume does for Great Britain exactly the same service that is filled by the so-called Handbook series in the United States. At the end of the volume one finds a practitioner's index of new pharmaceutical and dietetic preparations. All the information here published is supplied by the manufacturers without the slightest indication as to whether or not any of the claims made have been verified. Also as a supplement one finds a complete list of the British books published during the year and also new editions. Finally there are a directory of mental and other institutions and spas in Great Britain and a list of medical and scientific periodicals.

Illustration: Its Technique and Application to the Sciences. By Carl D. Clarke, M.A., Associate Professor of Art as Applied to Medicine, University of Maryland, Baltimore. Cloth. Price, \$5.50. Pp. 394, with 272 illustrations. Baltimore: John D. Lucas Company, Publishers, 1939.

Today medical illustration is a specialty with several branches. The author of this volume teaches art as applied to medicine in the University of Maryland and has had extensive experiences in all the illustrative technics, including medical drawing and painting, molding and casting, and photography. The present volume contains thirty-two chapters, which begin with a history of medical drawing and painting. Then come introductions to the elements of drawing, including full descriptions of materials, after which are chapters on surgery, pathology, chemical drawings, lettering, microscopic subjects and photography. The final chapter, which is not a biologic chapter, is a fundamental consideration of the reproduction of drawings. The book is magnificently illustrated and may be considered one of the best fundamental contributions thus far available in this field.

Lehrbuch der speziellen pathologischen Anatomie für Studierende und Ärzte. Von Dr. Eduard Kaufmann. Band II, Teil 1. Lieferung 2: Geschlechtsorgane. Anhang: Literaturangaben. Bearbeitet von H. Gbel und F. J. Lang. Ninth and tenth edition. Paper. Pp. 1361-1710; 279* 326*, with 137 illustrations. Berlin: Walter de Gruyter & Co., 1940.

This instalment of the ninth and tenth edition of Kaufmann's Pathologic Anatomy deals with the organs of reproduction including the mammary gland. The previous part was reviewed in *THE JOURNAL*, Feb. 4, 1939, page 468. The editors of the present instalment have done their work well. The original character of the book is maintained successfully. The text, clearly written and well arranged, abounds with references to the literature. The bibliography, closely printed, fills forty-seven pages, which eventually are to be bound with the bibliographies of other parts. The illustrations, all black and white, at times somewhat too diagrammatic, are instructive.

Studies on Codeine Addiction. By C. K. Himmelsbach, Howard L. Andrews, Robert H. Felix, Fred W. Oberst and Lowrey F. Davenport. Federal Security Agency, United States Public Health Service. Supplement No. 158 to the Public Health Reports. Paper. Price, 15 cents. Pp. 67, with illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1940.

This pamphlet, issued under the authority of the Federal Security Agency of the United States Public Health Service, reviews the available medical literature dealing with addiction to codeine and then reports some studies on this subject carried out at Fort Leavenworth, Kan., and at Lexington, Ky. A third part is devoted to a study of the effects of codeine on the electrical potentials of the cerebral cortex. Part four concerns the effects of codeine addiction on behavior; part five, the urinary excretion of codeine; and part six, the use of codeine for the control of tuberculous cough. The final portion of this report is on the significance of codeine as an addicting drug.

It seems to be well established that codeine has an addiction liability, even though the amount of codeine required to satisfy

and support a preestablished addiction to morphine is 5.2 times greater. The evidence seems to indicate that codeine gives less psychic satisfaction than morphine, but its action on the cortex does not differ essentially from that of morphine. Thus the investigators are convinced that the pharmacologic effects of codeine are of the same nature but of a lower order than morphine in all of its characteristics. The reduction in liability to addiction, although considerable, has not reached the point where this drug can be used liberally or indiscriminately over protracted periods. Attention is called particularly to the fact that large doses are used to control the cough in tuberculous patients and that this is both wasteful and inherently dangerous. The final conclusion of the authors is that "Codeine addiction does not result from the use of a bad thing but from the abuse of a very good thing."

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Industrial Blindness; Competency of Optometrist as Expert Witness.—Reeder sustained an injury to his right eye when it was struck by a piece of coal while he was working at a cutting machine in the Black Starr Coal Corporation's mine. He claimed that thereafter his vision in that eye was greatly impaired. He was awarded compensation for permanent loss of vision in one eye by the workmen's compensation board of Kentucky. From a judgment of the circuit court, Harlan County, Ky., affirming that award, the employer appealed to the Court of Appeals of Kentucky.

All the expert witnesses agreed that Reeder had a scar on his right eye, that his vision in that eye was 20/200 and that such vision constituted about 10 per cent of normal vision. Two physicians, eminent eye specialists or oculists, who had examined Reeder's eyes testified that the impairment of Reeder's vision was not due to the injury to his eye but that he was a psychoneurotic and that his loss of vision was "a matter of mind rather than a reality." They further stated that they had applied well known deceit tests but had been unable to detect malingering. However, an optometrist who had also examined Reeder's eyes was permitted to testify that in his opinion the loss of vision was due to the scar on the eye or to the injury causing it. On appeal, the appellant contended that the lower court had erred in admitting the optometrist's testimony because an optometrist is not qualified to testify as an expert witness as to causes of deficiency of vision. The Court of Appeals, however, pointed out that on being asked concerning his qualifications the optometrist in question had testified that he had long experience in the practice of his profession, that while the primary function of optometrists is the testing of eyes and the fitting of glasses they are also trained to recognize disease conditions of the eye; that he himself was trained and skilled in the examination for and the diagnosis of conditions of the eye but he did not give treatment, and that when treatment was indicated he sent his patients to a physician specializing in diseases of the eye. Also, when asked concerning matters of evidence about which the oculists had testified, he displayed general knowledge concerning the subject. In view of this evidence of training and experience the court was of the opinion that the optometrist was competent to testify as an expert witness. In so holding, the court relied on 22 C. J., page 52, note (d), and page 519, section 606, in which it is stated that when the occupation of a witness is such as to afford him special opportunity for acquiring knowledge and experience with respect to a kindred occupation and to render it probable that such knowledge and experience were acquired, the witness is competent to testify as to matters connected with the latter occupation. As was announced in *King v. King*, 161 Miss. 51, 134 S. W. 827, an expert witness need not be infallible or show the highest degree of skill but it is generally sufficient if he possesses peculiar

knowledge respecting the matters involved not likely to be possessed by ordinary laymen.

The appellant also contended that industrial blindness relates to the sight of both eyes and not to one eye only. While the Court of Appeals did not specifically pass on this question, it did so indirectly when it adopted the undisputed testimony of the two physicians and the optometrist that Reeder had sustained a loss of 90 per cent of the vision in his right eye and that such constituted "industrial blindness" in that eye.

Accordingly, the Court of Appeals affirmed the judgment of the circuit court upholding the award of compensation.—*Black Starr Coal Corporation v. Reeder* (Ky.), 128 S. W. (2d) 905.

Workmen's Compensation Acts: Aggravation of Pre-existing Heart Disease by "Unusual Effort" Compensation.—Rother, who was 53 years of age and had been afflicted with a heart condition for several years, was employed by the defendant company after examination by a physician. He was put to work unloading a freight car which contained crates of oranges weighing from 60 to 85 pounds. Sometime between one half and three quarters of an hour after he commenced to work he was found lying face down "breathing hard in a shivery manner, shaking." He died a few minutes thereafter. His widow, the claimant, filed a claim for compensation under the workmen's compensation act of New Jersey. The workmen's compensation bureau found that Rother's death was due to his employment in that unusual effort exerted by him had aggravated his preexisting heart condition and caused his death. The bureau awarded the claimant compensation, which award was affirmed by the court of common pleas of Hudson County, N. J. The employer then petitioned the supreme court of New Jersey for a writ of certiorari to review that judgment.

The only question that the supreme court was called on to decide was whether Rother had died solely as the result of a serious heart condition with which he had been afflicted for several years prior to his death or whether his death was the result of unusual effort necessarily expended in his work which had aggravated his preexisting heart condition. In the opinion of the court, the duties of Rother's employment did call for unusual effort, and the unusual exertion which he expended aggravated his preexisting heart condition with the result that he died of "syncope due to cardiac disease probably myocardial in nature." The court concluded that under such circumstances Rother's death rose out of and in the course of his employment and was therefore compensable. Accordingly, the supreme court refused to issue the writ of certiorari.—*Rother v. Merchants Refrigerating Co.* (N. J.), 6 A. (2d) 404.

Society Proceedings

COMING MEETINGS

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Excelsior Springs, Mo., Sept. 26-28. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.
American Association of Railway Surgeons, Chicago, Sept. 16-18. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.
American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.
American Hospital Association, Boston, Sept. 16-20. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.
American Roentgen Ray Society, Boston, Sept. 26-Oct. 4. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Canada, Secretary.
Colorado State Medical Society, Glenwood Springs, Sept. 11-14. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.
Idaho State Medical Association, Sun Valley, Sept. 11-14. Dr. J. N. Davis, 204 Fourth Ave., East, Twin Falls, Secretary.
Kentucky State Medical Association, Lexington, Sept. 16-19. Dr. A. T. McCormack, 620 South Third St., Louisville, Secretary.
Michigan State Medical Society, Detroit, Sept. 24-27. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing, Secretary.
Mississippi Valley Medical Society, Rock Island, Ill., Sept. 25-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.
National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
Oregon State Medical Society, Eugene, Sept. 4-7. Dr. Morris L. Bridgeman, 1020 S.W. Taylor St., Portland, Secretary.
Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
Wisconsin, State Medical Society of, Milwaukee, Sept. 18-20. Mr. J. G. Crownhart, 110 East Main St., Madison, Secretary.
Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery 9:365-408 (May) 1940

Some Contributions of Nutritional Research to Clinical Medicine. E. V. McCollum, Baltimore.—p. 365.

*Status Asthmaticus: Specific Chemotherapy in Treatment—Preliminary Report. C. K. Weil and H. J. Climo, Montgomery.—p. 370.

The Health Worker: How the Layman Looks on Him. E. V. Caldwell, Huntsville.—p. 374.

Community Health as Interpreted by a Private Practitioner. W. W. Alexander, Florence.—p. 377.

Status Asthmaticus.—Weil and Climo cite seven cases of status asthmaticus treated with sulfanilamide. Six of these responded promptly by rapid relief of symptoms. In the exception the sputum showed a preponderance of pneumococci but after treatment with sulfapyridine relief was prompt. One of the patients with chronic bronchitis and emphysema had staphylococci in his sputum but nevertheless he responded to sulfanilamide therapy. In this type of case sulfathiazole might be expected to give better results. The authors do not suggest that sulfanilamide and its derivatives will relieve all cases of status asthmaticus or that they will actually cure asthma. There may be cases of status asthmaticus which result from an overwhelming contact with some extrinsic substance of antigenic quality in which they do not know what effect sulfanilamide may have. In cases of status asthmaticus which result from respiratory infection, sulfanilamide and sulfapyridine seem to offer the possibility of dramatic relief. The authors do not yet feel certain about the optimal dose of sulfanilamide and its derivatives. They have used the following schedule for adults: 20 grains (1.3 Gm.) every six hours for two days, 15 grains (1 Gm.) every six hours for three days and 10 grains (0.65 Gm.) every six hours for seven days. There is still a question as to how long treatment should be continued. It is not known whether this method will be as efficacious in cases of chronic bacterial asthma or so-called bronchitis with asthma, even in the absence of status asthmaticus. The principles underlying the two conditions are similar and should respond to similar therapy. This method of treating status asthmaticus may afford relief to some patients with less prolonged hospitalization and less expensive medication than has been possible in the past. When the indications for the use of these drugs, the proper dosage and the duration of treatment have been well established, the outlook for the asthmatic patient may be improved considerably and the late complications of asthma—chronic bronchitis, bronchiectasis, emphysema, pulmonary fibrosis, cardiac hypertrophy and myocardial damage—prevented.

American Journal of Cancer, New York 39:1-148 (May) 1940

Histologic Analysis of Tumors: Critical Review. L. Foulds, London, England.—p. 1.

Spontaneous Primary Hepatomas in Mice of Strain C3H: Study of Incidence, Sex Distribution and Morbid Anatomy. E. L. Burns and J. R. Schenken, New Orleans.—p. 25.

Transplantable Carcinoma of Rat Breast. M. J. Eisen, New York.—p. 36.

Investigations on New Heterologous Tumor, "Budapest 1938," Successfully Propagated in Hungarian White Rats. E. de Balogh, Budapest, Hungary.—p. 45.

Development of Sarcoma in Mice Following Long Continued Injections of Buffered Solution of Hydrochloric Acid. V. Szentzeff, R. S. Babcock and L. Loeb, St. Louis.—p. 56.

Stomach Lesions in Rats Kept on Diets Deficient in Vitamin A. L. S. Fridericia, S. Gudjonsson, B. Vinterup, S. Clemmensen and J. Clemmensen, Copenhagen, Denmark.—p. 61.

Volume of Injection and Concentration of Carcinogenic Chemical as Factors in Initiation of Malignant Process and Their Bearing on Somatic Mutation Hypothesis. W. F. Dunning, M. R. Curtis and F. C. Wood, New York.—p. 70.

Tumor Incidence in Line A Albino Mice Following Injections of Progynon-B. E. Elizabeth Jones, Brookline, Mass.—p. 94.

Glycolysis of Erythrocytes During Tumor Growth. H. Werner and A. Kleinzeller, Brno, Czechoslovakia.—p. 100.

Possible Method of Transmission of Susceptibility to Breast Cancer in Mice. J. J. Bittner, Bar Harbor, Maine.—p. 104.

American Journal of Diseases of Children, Chicago 59:1167-1438 (June) 1940

*Clinical Studies of Vitamin A in Infants and in Children. C. D. May, K. D. Blackfan, Boston; J. F. McCreary, Toronto, and F. H. Allen Jr., Holyoke, Mass.—p. 1167.

Respiratory Metabolism in Infancy and in Childhood: XXIII. Daily Energy Requirements of Premature Infants. H. H. Gordon, S. Z. Levine, W. C. Deamer and H. McNamara, New York.—p. 1185.

Distorted Speech in Young Children. L. W. Karlin, Adella C. Youtz and Lou Kennedy, Brooklyn.—p. 1203.

Effect of Irradiation of Air in Ward on Incidence of Infections of Respiratory Tract. L. H. Barenberg, D. Greene and L. Greenspan, New York.—p. 1219.

VIII. Background and Social Adjustment of Thyroid Deficient Children Receiving Glandular Therapy. Joyce W. McDonald, A. W. Brown and I. P. Bronstein, Chicago.—p. 1227.

Transitory Synovitis of Hip Joint in Children. S. Rauch, Brooklyn.—p. 1245.

*Duration of Immunity to Diphtheria Achieved by Toxin-Antitoxin and Alum Precipitated Toxoid. W. B. Nevius and Ada C. McGrath, East Orange, N. J.—p. 1266.

Cirrhosis of Liver in Children. G. T. Harrell and A. McBryde, Durham, N. C.—p. 1301.

Vitamin A in Children.—May and his associates describe a photoelectric colorimeter technic, using selective light filters, for the quantitative estimation of vitamin A and the carotenoids in small amounts of blood serum. With the technic (1) the rapidly changing blue color may be read instantly at its maximum, (2) subjective error is eliminated, (3) selective light filters allow for correction due to blue color arising from the carotenoids, (4) carotenoids and vitamin A may be determined with the same aliquot of extract, (5) the small amounts of color obtainable from 1 cc. of blood serum can be measured accurately and (6) the entire procedure is simple to perform. Its accuracy and dependability were indicated by the results obtained when duplicate analyses for carotenoids and vitamin A were done on separate specimens of the same blood. By means of the technic, normal well nourished children from birth to 12 years of age were found to have levels of vitamin A in their blood ranging from 5.5 to 27.3 units. The levels of carotenoids also covered a wide range, from 3.1 to 75.7 units. The wide range of values is not confusing, as the alterations in the levels of vitamin A and carotenoids in pathologic states are beyond the limits seen under normal circumstances. In acute infections with fever, the blood levels of both vitamin A and carotenoids decrease. The levels may rise spontaneously to normal during the subsidence of the infection. As the bodily stores of vitamin A are depleted the carotenoids in the blood decrease, and not until these have become considerably lowered does the level of vitamin A begin to fall. In some of the infants whose intake of vitamin A and carotenoids was restricted, the levels in the blood dropped considerably below the lowest limits of normal. The low levels in the blood were the only clue to a deficiency of vitamin A and dropped before the appearance of cornified epithelial cells in the conjunctiva and respiratory and genito-urinary tracts. The authors' studies indicate that the vitamin A customarily supplied to infants in ordinary whole cow's milk formulas may be scarcely sufficient to maintain an optimal level of vitamin A in the blood. If the absorption of vitamin A from the intestine is impaired, depletion of the bodily stores and lowering of the level in the blood may be expected, even when the vitamin A intake is normal. The study of intestinal absorption has been facilitated by the utilization of a vitamin A absorption test (Chesney and McCoord, 1934). Failure of the level to rise to normal after ingestion of vitamin A (0.1 cc. of peracemorph liver oil per pound of body weight) used in the absorption test may be assumed to indicate a decrease in intestinal absorption. Impaired intestinal absorption has been found in congenital obliteration of the bile ducts, fibrosis of the pancreas, celiac disease and cretinism, in which the average rise was 8.2 units after absorption test doses as compared to 129.7 units in normal children. There is no advantage in parenteral administration of the vitamin. The defect in absorption may be easily overcome by the

oral administration of unusually large amounts of vitamin A, preferably in divided doses. The presence of a low absorption curve is an indication for the administration of large amounts of vitamin A if normal levels are to be maintained and deficiency prevented.

Duration of Immunity to Diphtheria.—Nevius and McGrath compared the results of Schick tests on groups of school children five years after immunization with toxin-antitoxin and with alum precipitated toxoid. Seventy-eight children who had been given three 1 cc. doses of diphtheria toxin-antitoxin in 1932 and who had negative Schick reactions one year later were again given the Schick test in 1937 and seventy-five, or 96 per cent, still reacted negatively. Of seventy-two children who were given 1 cc. of alum precipitated toxoid in the fall of 1933 and had negative Schick reactions in 1934 only fifty-eight children, or 80 per cent, still reacted negatively in the fall of 1938. It appears that, while alum precipitated toxoid produces a prompt negative Schick reaction in a high percentage of cases, the result is transient and disappears after five years in about 20 per cent of children. The study bears out the general belief that the immunity from a single dose of 1 cc. of alum precipitated toxoid does not last as long as that from the older preparations. This should encourage the use not of the older toxin-antitoxin preparations but of two 1 cc. doses of alum precipitated toxoid two or three weeks apart and Schick retesting of the children at regular intervals. Since the ideal time for immunization of the infant is when he is between 6 and 9 months of age, Schick tests should be done at the ages of 12 months, 3 years and 5 years or just before the child enters school. In the event that the reaction becomes positive, another 1 cc. dose of toxoid should be given with subsequent retesting.

American J. Obstetrics and Gynecology, St. Louis

39:919-1102 (June) 1940. Partial Index

- Some Sociologic and Psychologic Observations on Abortion: Study of 537 Cases. Virginia Clay Hamilton, New York.—p. 919.
- Weight Changes During Pregnancy and Puerperium. H. J. Stander and J. B. Pastore, New York.—p. 928.
- *Clinical Study of Stilbesterol. M. E. Davis, Chicago.—p. 938.
- Endometriosis: Study of 260 Private Hospital Cases. R. Fallas and G. Rosenblum, Los Angeles.—p. 964.
- Pseudo-Uterus Arcuatus and Functional Malformations of Uterus: Their Effect on Pregnancy and Parturition. L. Rudolph, Chicago.—p. 975.
- Experiment in Cancer Control: Preliminary Report on Periodic Pelvic Examinations of 1,000 Well Women. Catharine Macfarlane, Faith S. Fetterman and Margaret C. Sturgis, Philadelphia.—p. 983.
- Study of Incidence of Syphilis in Pregnant Women and Some Results of Therapy. V. Moseley, J. L. Callaway and Jane Stiles Sharpe, Durham, N. C.—p. 990.
- *Results of Treatment in Carcinoma of Uterine Cervix. R. W. Teahan and H. Wammock, Philadelphia.—p. 995.
- *Observations on Pathology of Trichomonas Vaginitis and on Vaginal Implants with Trichomonas Vaginalis and Trichomonas Intestinalis. J. F. Kessel and J. A. Gafford Jr., Los Angeles.—p. 1005.
- Coexistence of Carcinoma and Tuberculosis of Uterus. J. M. Ravid and E. Scharfman, Brooklyn.—p. 1025.
- Appraisal of Routine Use of Special Postpartum Exercise. W. B. D. Van Auker, Troy, N. Y.—p. 1032.
- Blood Phosphatase in Pregnancy an Indication of Twins: Preliminary Report. J. H. Ebbs and W. A. Scott, with technical assistance of W. M. Johnstone, Toronto.—p. 1043.
- Oral Administration of Stilbesterol. J. C. Weed, B. B. Weinstein, F. R. Lock, J. W. Douglas and C. G. Collins, New Orleans.—p. 1047.
- Carcinoma of Cervix in 7 Months Old Infant. E. G. Waters, Jersey City, N. J.—p. 1055.
- Acute Anterior Poliomyelitis Complicating Carcinoma of Cervix in 30 Year Old Female. L. Litter and H. Strauss, Brooklyn.—p. 1058.
- Friedman Tests with Ovarian Pregnancy. C. H. Davis and Verna Stevens-Young, Wilmington, Del.—p. 1063.
- Cancer of Cervix in Virgin with Intact Hymen. A. F. Lash, Chicago.—p. 1070.

Stilbesterol.—Davis used stilbesterol in the treatment of 100 women with menopausal symptoms. Each patient received 1 mg. of stilbesterol at bedtime and this was sufficient to control the symptoms. About 20 per cent of the women who at first were given 5 mg. of stilbesterol daily complained of nausea, with or without vomiting, or of an uncomfortable sensation in the abdomen. When the daily dose was reduced to 1 mg., most of these women could tolerate the medication without any discomfort. In only three instances did the morning nausea and the upset feeling persist. Ninety-three of the 100 women were completely relieved of their menopausal symptoms, hot flushes, headaches, tenseness at the back of the head and neck muscles, nervous manifestations,

hyperexcitability, irritability and mental depression. The menopausal symptoms of four women were only partly relieved. Two of these took the drug intermittently. Twelve women in the group had been treated with the natural estrogens by parenteral administration. Some of these patients had fairly complete relief from symptoms but most of them had little relief but continued treatment because it was the best therapy that could be offered. It was difficult to substitute oral medication for the hypodermic injections, but the improvement that followed stilbesterol convinced all but one woman that the change was a desirable one. These women were rapidly freed from all their flushes and of most of the other concomitant complaints. Medication must be continued until the symptoms begin to wane or disappear. After several months of medication the amount of the drug can be reduced. If symptoms return the daily dose should be increased. A sudden cessation of therapy is often followed by vaginal bleeding within ten to twenty days. This is the characteristic withdrawal phenomenon. Stilbesterol was the ideal estrogen for the treatment of two cases of primary amenorrhea, with its attendant underdevelopment of secondary sex characteristics. The daily oral administration of 1 mg. of the drug was sufficient to produce physical and sexual maturity. The changes induced in these patients in a month were truly astounding. The prepubertal state was rapidly replaced by the physical and organic development of the mature woman. All the secondary sex characters developed. The reproductive organs assumed the normal adult type. All this was accomplished in several months, whereas normal adolescence requires three or four years. The gonads were the only reproductive organs that were not affected and remained dormant. These young women remain normal only if treatment is continued. Only careful clinical observations and experimental studies over long periods will determine the desirability of continued treatment and its safety. The amount of stilbesterol necessary to maintain the optimal development of the individual must be ascertained. About 1 mg. daily has been sufficient to prevent regression, but it is possible that this amount is too large. Careful endocrine assays may reveal the optimal daily consumption of this drug. Bleeding, with some degree of regularity, occurs from seven to twenty days following withdrawal of the drug as well as on continued medication. The only difference between true ovulatory menstruation and these anovulatory bleedings is in the endometrial picture, which resembles that prior to ovulation. The bleeding is preceded by the usual premenstrual prodromes. The blood loss is scanty in amount and there is no loss of desquamated endometrial fragments. Cutaneous pigmentation occurs and is most marked in the nipples and the areolas, but the linea alba as well as other mildly pigmented areas become intensely discolored. The nature of this pigmentation is being studied.

Results of Treatment in Carcinoma of Cervix.—From 1928 to 1937 Teahan and Wammock saw 229 cases of carcinoma of the uterine cervix; 136 of these were seen before Dec. 1, 1934, and therefore have been observed for five years or more. Treatment has been exclusively by irradiation with x-rays and radium. Of the 136 patients, 122 were treated and twenty-six survived five years or more. The absolute cure rate is 19.1 per cent and the relative cure rate 21.3 per cent. Treatment of sixty-nine patients was initiated by the authors and the five year cure rate in this group is 33½ per cent. Of the fifty-three patients who had received some treatment elsewhere, the disease was either not controlled or it recurred. These patients were given more treatment, but only three (5.7 per cent) survived five years. Not all patients received combined roentgen and radium therapy. In some of the advanced cases the use of radium appeared to be contraindicated. Fifty-one patients received the combined x-rays and radium, and the five year cure rate in this group is 37.3 per cent. Vesicovaginal fistulas developed in two patients of this group. Four fistulas occurred among the patients receiving an incomplete cycle of treatment. Ten fistulas occurred among those patients who received their initial treatment elsewhere, and one in a patient receiving no treatment. It appears that, except for the extent of the disease, the initial treatment is the most important factor in determining the ultimate result. Inquiry showed that, while the patient is consulting a physician more promptly after the appearance of the initial sign, the interval between the first visit and the first pelvic examination does not appear to be shortened.

Pathology of Trichomonas Vaginitis.—Kessel and Gafford state that serial sections of biopsies from areas of hemorrhage and granulation from cases diagnosed as trichomonas vaginitis indicate that the pathologic change is not produced alone by simple invasion of flagellates from the lumen of the vagina but that some additional mechanism exists, either toxic or bacterial in nature, which is partially responsible for primary tissue changes. Implants into normal vaginas of exudate from cases of trichomonas vaginitis containing *Trichomonas vaginalis* and bacteria resulted in the occurrence of characteristic vaginitis, while implants of cultures of *Trichomonas vaginalis* and bacteria produced only one case of typical vaginitis and implants of *Escherichia coli* and an alpha streptococcus in culture produced only a mild vaginitis without characteristic discharge. Experimental implants of *Trichomonas vaginalis* to human and monkey vaginas resulted in infection, while attempts to infect human and monkey vaginas with *Trichomonas intestinalis* ended with negative results. The study fails to support the theory that the trichomonads which infect the vagina are of intestinal origin. The evidence supports the theory that *Trichomonas vaginalis* and *Trichomonas intestinalis* (*Trichomonas hominis*) are distinct species, since they exhibit both morphologic and environmental differences.

American Journal of Pathology, Boston

16:237-374 (May) 1940. Partial Index

- Spontaneous Tumors in Two Colonies of Rats of the Wistar Institute of Anatomy and Biology. H. L. Ratcliffe, Philadelphia.—p. 237.
Morphologic Alterations in Gasserian Ganglion Cells and Their Association with Senescence in Man. R. C. Truex, Minneapolis and New York.—p. 255.
Physiologic Hypertrophy of Parathyroids, Its Cause and Its Relation to Rickets. A. W. Ham, N. Littner, T. G. H. Drake, E. C. Robertson and F. F. Tisdall, Toronto.—p. 277.
Studies in Carcinogenesis: IX Hydrocarbon-Cholesterol Pellets in Strain D Mice. M. J. Shear, Cambridge, Mass., and F. W. Ilfeld, Boston.—p. 287.
Id.: X. Production of Tumors by 3:4-Benzpyrene in Rats Fed Diets Containing Different Levels of Vitamin A. P. R. Howe, M. D. Elliott, Boston, and M. J. Shear, Cambridge, Mass.—p. 295.
Id.: XI. Development of Skin Tumors in Mice Painted with 3:4-Benzpyrene and Creosote Oil Fractions. S. Cahot, Boston; N. Shear and M. J. Shear, with technical assistance of A. Perrault, Cambridge, Mass.—p. 301.
Metastatic Neuroblastoma in Bone Presenting Ewing Syndrome, with Discussion of "Ewing's Sarcoma." R. A. Willis, Victoria, Australia.—p. 317.
Meningococcal Endocarditis and Myocarditis: Report of Case with Unusual Lesions in Arterial Tree. M. G. Whillans, Toronto.—p. 365.

Archives of Internal Medicine, Chicago

65:1085-1314 (June) 1940

- Insulin and Cerebral Damage. F. Klein and J. A. Ligterink, Groningen, Netherlands.—p. 1085.
Dissecting Aneurysm of Aorta. J. A. Reisinger, Washington, D. C.—p. 1097.
*Hyperthyroidism and Diabetes. J. F. Regan and R. M. Wilder, Rochester, Minn.—p. 1116.
Clinical Manifestations of Paroxysmal Hypertension Associated with Pheochromocytoma of Adrenal: Report of Proved and of Doubtful Case. E. F. Van Epps, O. R. Hyndman and J. A. Greene, Iowa City.—p. 1123.
*Clinical Value of Determination of Cholesterol Esters of Blood in Hepatic Disease. C. H. Greene, R. Hotz and Evelyn Leahy, New York.—p. 1130.
Treatment of Pneumonia with Sulfapyridine: Observations on Toxic Reactions. H. K. Detweiler, H. I. Kinsey, W. H. Brown and W. R. Feasby, Toronto.—p. 1144.
*Purpura Haemorrhagica Following Neoarsphenamine and Bismarsen Therapy: Further Studies on Sensitivity to Arsphenamine and Tolerance to Mapharsen. E. H. Falconer and N. N. Epstein, San Francisco.—p. 1158.
Degenerative Lesions in Cervical Portion of Spine. T. Horwitz, Philadelphia.—p. 1178.
Glomerular Nephritis Following Infections of Skin. P. H. Futeher, New York.—p. 1192.
Blood: Review of Recent Literature. R. Isaacs, C. C. Sturgis, F. H. Bethell and S. M. Goldhamer, Ann Arbor, Mich.—p. 1211.

Hyperthyroidism and Diabetes.—Regan and Wilder add sixty-one cases of hyperthyroidism and diabetes to the thirty-eight that Wilder reported in 1926. They state that during the twelve years between the reports the incidence of frank diabetes as a complication of hyperthyroidism increased from 1.1 per cent to 3.2 per cent. As in the first report, its occurrence is more frequent in adenomatous goiter with hyperthyroidism (5.6 per cent) than in exophthalmic goiter (1.7 per cent). The fact that exophthalmic goiter occurs in younger

patients may partially explain this discrepancy. Patients with exophthalmic goiter generally seek medical attention earlier than do those with the more insidious form of hyperthyroidism accompanying adenomatous goiter. Therefore, more opportunity for precipitating diabetes is given by adenomatous goiter with hyperthyroidism. Owing to the uncertain onset of each disease and to the fact that certain symptoms (bulimia, loss of weight and weakness) are common to the two conditions, satisfactory conclusions frequently could not be reached as to the priority in the appearance of the two diseases. That the hyperthyroidism preceded in many cases is, however, quite clear. Nineteen of the sixty-one patients were encountered in a series of 1,132 patients with exophthalmic goiter seen at the clinic from 1935 to 1937 inclusive and forty-two among 750 patients who had adenomatous goiter with hyperthyroidism. In the latter group hyperthyroidism was a factor of etiologic significance in the precipitation of the diabetes. A follow-up of Wilder's thirty-eight patients who had hyperthyroidism with diabetes shows that when those who did not have thyroidectomy are excluded the average duration of life after the onset of diabetes was 12.4 years. The data support the assumption that patients with hyperthyroidism and diabetes who receive satisfactory surgical treatment for their hyperthyroidism do as well as patients with diabetes alone, whereas those who are not relieved by operation fare badly.

Cholesterol Esters of Blood in Hepatic Disease.

Greene and his associates determined the clinical value of the ratio of combined to total cholesterol in the blood of 645 patients with possible disease of the liver or of the extrahepatic biliary tract. After the routine total and combined cholesterol determinations, icteric index and van den Bergh test on each patient and an adequate follow-up period, 598 of the 645 patients were found to have no apparent hepatic damage. The normal range of total cholesterol was found to be from 150 to 230 mg. per hundred cubic centimeters and that of the esters from 60 to 120 mg. The ratio of combined to total cholesterol was 46 per cent plus or minus 6. One hundred and fifty-four determinations of the total cholesterol and of the cholesterol esters in the blood were made on the forty-seven patients with proved hepatic disease or biliary obstruction of hepatic origin. The results showed that there was a marked "shift to the left" of the values for patients with hepatic disease. The thirty-one patients with hepatic disease showed the greatest decreases in esters. The esters were not definitely decreased in the sixteen patients with obstructive jaundice, although the ratio had a tendency to be lower than the 40 per cent determined as the lower normal limit. There was a general increase of total cholesterol in the blood of patients with obstructive jaundice, but in hepatic disease the cholesterol esters tended to disappear from the blood regardless of the behavior of the total cholesterol. A progressive decrease in the values for the combined cholesterol of the blood signifies a poor prognosis and vice versa. The combined cholesterol determination is of great value in determining the prognosis after surgical intervention for disease of the biliary tract.

Hemorrhagic Purpura Following Treatment with Arsenicals.—Since 1936, Falconer and Epstein have encountered six patients with hemorrhagic purpura following treatment with arsphenamine derivatives. Five of the patients showed typical hemorrhagic purpura following the use of neoarsphenamine or of bismarsen but had no apparent reaction following the intravenous injection of mapharsen. The sixth patient showed large ecchymotic areas in the skin but no thrombopenia following the administration of bismarsen and neoarsphenamine. The authors believe that the condition is of much more frequent occurrence than published reports would indicate. Seven of the eight patients (two reported in 1936) have been tested for tolerance to mapharsen, and none have shown any untoward reaction or any evidence of hemorrhagic purpura following its use. Varying degrees of shock occurred after test doses of arsphenamine to which five of the patients of the present series were sensitive. This suggests that the reaction was an allergic phenomenon rather than one due to the toxic effects of oxidation or to a changed chemical form of the drug injected. The prompt loss of circulatory tone accompanying the reaction appears to be a vasomotor effect, with loss of capillary tonus, dilatation of the capillary bed and a rapid loss of platelets from the general

circulation. It is difficult to believe that such enormous numbers of platelets could be destroyed within fifteen minutes after the drug was injected. The fact that a great number of platelets were returned promptly into the general circulation by the injection of 1 cc. of epinephrine hydrochloride (1:1,000 solution) and that the count rose within twenty-four to forty-eight hours after the reaction is evidence against the assumption of widespread destruction of the platelets. Blood cells other than the platelets showed little if any change. There appeared to be a tendency to an increase of the polymorphonuclear cells following a reaction, particularly a severe reaction. This may well be a phenomenon similar to the leukocytosis associated with protein shock.

Archives of Pathology, Chicago

29:741-892 (June) 1940

- Experimentally Induced Benignancy of Neoplasm: IV. Suppression of Mitotic Activity by So-Called Immunization. A. M. Brues and W. T. Salter, Boston.—p. 741.
Alveolar Lining of Lung in Relation to Viability of Fetus. Mary Zeldes, Chicago.—p. 748.
Golgi Apparatus of Thyroid Gland. C. S. Welch and A. C. Broders, Rochester, Minn.—p. 759.
Chemotactic Properties of Tuberculophosphatide and Tuberculopolysaccharide. W. B. Wartman and E. S. Ingraham Jr., Cleveland.—p. 773.
Histologic Changes in Renal Arterioles of Hypertensive Rabbits. F. W. Dunihue and B. H. Candon, Burlington, Vt.—p. 777.
Effects of Thyroid and Calcium Therapy on Growth of Sarcoma Transplants in Thyroparathyroidectomized Rats. R. L. Ferguson, R. D. Templeton, Mary C. Patras and F. A. McJunkin, Chicago.—p. 785.
Experimental Gastric Carcinoma: Critical Review with Comments on Criteria of Induced Malignancy. A. J. Klein and W. L. Palmer, Chicago.—p. 814.

Bulletin New York Academy of Medicine, New York

16:345-428 (June) 1940

- Adrenal Insufficiency. R. F. Loeb, New York.—p. 347.
The Cushing Syndrome: Neoplasms of Adrenal Gland. S. Silver, New York.—p. 368.
Surgical Considerations in Treatment of Chronic Lymphedema and of Varicose Veins. G. H. Pratt, New York.—p. 381.
Mechanism of Allergy. M. Walzer, Brooklyn.—p. 389.
Allergy in Childhood. L. W. Hill, Boston.—p. 395.
Analysis of Maternal Deaths and Hospital Obstetric Statistics in New York County. M. Schneider, T. J. Duffield and Sylvia L. Parker, New York.—p. 404.

Canadian Medical Association Journal, Montreal

42:521-628 (June) 1940

- Fractures of Mandible. S. Gordon, Toronto.—p. 521.
Skin Test for Susceptibility to Pertussis. L. P. Streat, Montreal.—p. 525.
Granuloma Pyogenicum: Report of Four Cases Treated by Roentgen Rays. D. Eisen, Toronto.—p. 528.
Unilateral Multilocular Cystic Kidney: Report of Case in Young Child. W. A. Dakin, Regina, Sask.—p. 531.
Treatment of Gonorrhea by Chemotherapy: Preliminary Note. D. R. Mitchell, C. H. Greig and J. L. Uren, Toronto.—p. 533.
Backache: Relation of Physical Therapy to Its Management. F. H. Krusen, Rochester, Minn.—p. 534.
*Hemorrhagic Tendency Associated with Prothrombin Deficiency and Its Treatment with Vitamin K and Bile. S. R. Townsend and E. S. Mills, Montreal.—p. 541.
Relative Merits of Intravenous and Retrograde Urograms. G. S. Foulds and E. H. Shannon, Toronto.—p. 547.
Effect of Reducing Diets on Eye: A Public Health Problem. W. Thau, Boston.—p. 550.
Survey of Ophthalmic Conditions Among Rural School Children. J. V. V. Nicholls, Montreal.—p. 553.
Induction of Labor. W. P. Tew, London, Ont.—p. 556.
Management of Delayed Labor. G. C. Melhado, Montreal.—p. 562.
Recognition of Late Toxemia of Pregnancy in Its Incipience. H. F. Dyer, Hamilton, Ont.—p. 565.
Hysterosalpingography in Diagnosis of Gynecologic Affections. J. E. Gendreau and O. Dufresne, Montreal.—p. 567.
Appendicitis. R. M. Wansbrough, Toronto.—p. 568.
Treatment of Carcinoma of Colon. R. V. B. Shier, Toronto.—p. 570.

Vitamin K and Bile for Hemorrhagic Tendency.—Townsend and Mills compare the results in eighteen cases of jaundice in which treatment with vitamin K was not given with those of seventeen in which vitamin K and bile were given and three in which synthetic vitamin K preparations were given. There were three deaths from hemorrhage in the untreated group as compared to no fatalities in the other group. Three of the twenty treated patients bled postoperatively. Vitamin K and bile therapy resulted in a prompt beneficial effect. None of the patients bled before operation. Many of the disturbances in

prothrombin time were considerably prolonged but were restored to normal with adequate vitamin K treatment. The oral administration of 3,000 units (approximately 90,000 Dam units) of vitamin K daily with from 2 to 3 Gm. of desiccated whole fresh bile is sufficient to reduce the prothrombin time to normal in three days. Smaller dosage requires a longer time and conversely larger dosage a shorter interval to produce a comparable result. The authors' experience with synthetic vitamin K indicates that these substances may prove more potent than the original vitamin K preparations from alfalfa, and that this new therapy will replace the early type of treatment. In the three cases studied there were no local reactions or toxic effects. Blood studies revealed no evidence of a hemolytic anemia, but this complication should be kept in mind until more is known of the action of these substances in man. Cases were treated effectively by both the oral and parenteral methods. The latter has the advantage of being effective without bile and is uninfluenced by factors affecting absorption from the gastrointestinal tract. From 1 to 2 mg. of the synthetic vitamin K substitutes daily have proved effective. Treatment was equally effective in other conditions associated with prothrombin deficiency, such as gastrointestinal lesions without jaundice, and in cases in which infection seemed to be the only factor. No definite relationship was found between the degree of disturbance of the prothrombin time and the duration or intensity of the jaundice. This was considered to be due to the fact that many cases did not show complete obstruction as indicated by the low values of the plasma bilirubin.

Georgia Medical Association Journal, Atlanta

29:295-340 (June) 1940

- Reminiscences of a Georgia Pediatrician. S. A. Visanska, Atlanta.—p. 295.
Two Case Reports of Interest from the Diagnostic Standpoint. P. S. Kemp, Macon.—p. 321.

Journal-Lancet, Minneapolis

60:253-290 (June) 1940

- Pollinosis: From Standpoint of Preventive Medicine and Public Health. R. V. Ellis, Minneapolis.—p. 253.
Bowel Obstruction at Birth. E. M. Miller, Chicago.—p. 258.
Care of Severe Injuries of Face and Jaws. J. B. Brown and F. McDowell, St. Louis.—p. 260.
Intra-Ocular Malignancies. W. H. Fink, Minneapolis.—p. 268.
Interrelationships of Health and Physical Education. J. E. Raycroft, Princeton, N. J.—p. 270.
Paranasal Sinusitis: Factors in Management and Prognosis. F. L. Bryant, Minneapolis.—p. 273.
Relationship of Physical Education to Health Service. L. C. Boles, Wooster, Ohio.—p. 278.
Tuberculosis in Nursemaids. D. V. Sharp, Minneapolis.—p. 280.
Abscesses of Neck: Case Reports. H. P. Rosenberger, Bismarck, N. D.—p. 281.

Journal of Pediatrics, St. Louis

16:679-828 (June) 1940

- Intravenous Administration of Small Doses of Casein Hydrolysate to Nephrotic Children and Its Effect on Nitrogen Balance and Plasma Amino Acid Level. L. E. Farr, New York.—p. 679.
Acacia Therapy in Child with Nephrosis. Dorothy F. Falkenstein and R. L. Jackson, Iowa City.—p. 700.
Synthesized, Processed and Natural Sources of Vitamin C in Mineral Metabolism of Normal Children. Marion L. Shepherd, Icie G. Macy, Helen A. Hunscher and Frances Cope Hummel, with assistance of Mary Bates Olson, Priscilla Bonner, J. Horton, A. Theresa Johnston and Louise Emerson, Detroit.—p. 704.
*Survey of State of Nutrition with Respect to Vitamin C in a Southern Pediatric Clinic. Ann S. Minot, Katharine Dodd, Margaret Keller and Helen Frank, Nashville, Tenn.—p. 717.
Some Responses of Child to Exercise. F. W. Schlutz, Minerva Morse and J. L. Gedgoud, Chicago.—p. 729.
Congenital Arteriovenous Fistulas in Children. C. E. Ward and B. T. Horton, Rochester, Minn.—p. 746.
Tonic Neck Reflex in Newborn Infants. Julia Mehlman, New York.—p. 767.
Thyroid Therapy in Juvenile Myxedema. L. G. Rowntree, Philadelphia.—p. 770.
Environmental and Personality Problems in Treatment of Diabetic Children. H. F. Shirley, San Francisco, and Ina May Greer, Iowa City.—p. 775.

Nutrition and Vitamin C.—Minot and her associates estimated the ascorbic acid in the blood serum of 533 children who came to the pediatric clinic for immunization, routine examination or specific treatment. The group consisted of 380 children with no serious complaint or disease, 105 sick children without

diarrhea and forty-eight sick children with diarrhea as the chief complaint. The data obtained in the first or normal group of children was subdivided into observations made from February 1 to June 1 and from June 1 to October 1, when fresh vegetables and fruits were more plentiful. The data show that there is considerable undernutrition with respect to vitamin C among the clinic group in this locality. During the months in which fresh fruit and vegetables are scarce, about 60 per cent of the children had levels of ascorbic acid below the generally accepted satisfactory level of 0.7 mg. per hundred cubic centimeters of serum and about 30 or 40 per cent less than 0.3 mg. During the months when fruit and vegetables are plentiful and cheap there was an obvious shift in distribution in older children. A considerably larger percentage reached a satisfactory level. Only about 10 per cent still gave evidence of gross undernutrition with respect to vitamin C. The seasonal variation was slight in children less than 3 years of age. Many more of the 105 sick than the normal children had frankly low levels of ascorbic acid in the serum. The highest percentage (62.5) of values below 0.3 mg. was found in the younger age group as against 31.2 per cent of children from 3 to 15 years of age. No particular disease influenced the level of vitamin C. The general trend to lower concentrations of ascorbic acid in the serum in the presence of disease indicates that special efforts are necessary if normal concentrations are to be maintained in sick children, especially if ascorbic acid plays the indispensable part it is believed to assume in normal biologic processes. All but three of the forty-eight sick children with diarrhea as the chief complaint were hospitalized and all except four were less than 3 years of age. The percentage of values less than 0.3 mg. of ascorbic acid per hundred cubic centimeters was essentially the same as in sick children less than 3 years of age without diarrhea. Failure to take food and poor absorption probably are more important factors in causing the low levels in the children with diarrhea. From 10 to 20 mg. per kilogram of ascorbic acid for one week or longer was frequently inadequate to restore or to maintain a satisfactory level of ascorbic acid in the serum of young children with severe diarrhea. The same doses usually suffice to restore the level in normal children of similar age. Whatever the cause of the deficiency, it is again apparent that young sick children with or without diarrhea are frequently deficient in vitamin C unless the extra required amount is supplied. The authors conclude that it is still not known why clinical evidence of scurvy is so seldom seen among the rather large group which is apparently grossly deficient in vitamin C. They suggest that diets which are simultaneously deficient in calories and other essential factors may suppress the typical manifestations of the deficiency but that in otherwise adequately nourished persons such diets would cause outspoken scurvy.

Journal of Pharmacology & Exper. Therap., Baltimore

69:103-176 (June) 1940. Partial Index

- Circulatory Effects of Venom of the Indian Cobra (*Naia Naia*). F. Gottdenker, São Paulo, Brazil, and M. Wachstein, New York.—p. 117.
Relation of Atropine to Adrenalin and Sympathetic System. L. J. Russell, Oxford, England.—p. 128.
Clinical Experiences with Some Curare Preparations and Curare Substitutes. M. S. Burman, New York.—p. 143.
In Vitro Action of Certain Sulfanilamide Derivatives on PR-8 Strain of Influenza Virus. D. R. Climenko, Bound Brook, N. J.—p. 165.
Comparative Therapeutic Activity of Sulfanilamide, Sulfapyridine, Sulfathiazole and Diaminosulfone in Type I Pneumococcus Infections in Mice. J. T. Litchfield Jr., H. J. White and E. K. Marshall Jr., Baltimore.—p. 166.

Kentucky Medical Journal, Bowling Green

38:231-278 (June) 1940

- Pituitary Adenoma and X-Ray Therapy of the Disease. H. Newman, Bowling Green.—p. 232.
Resistant, Recurrent and Metastatic Carcinoma. D. Y. Keith, Louisville.—p. 235.
Prolapsus Uteri. M. Casper, Louisville.—p. 240.
Historical Research. K. W. Rawlings.—p. 242.
Psychotherapy. S. Ackerly, Louisville.—p. 251.
The Army Medical Library of Washington and Its Collection of Early Kentuckiana. E. E. Hume, Washington, D. C.—p. 258.
Review of Acute and Chronic Arthritis. T. A. Griffith, Mount Vernon.—p. 268.
Intra-Uterine Skull Fracture. G. F. Jones and W. L. O'Nan, Henderson.—p. 273.

Maine Medical Association Journal, Portland

31:151-190 (June) 1940

- Benign Gastric Tumor: Report of Two Cases. I. M. Webber and W. D. Anderson, Portland.—p. 151.
Bingham Hospital Extension Services. J. Gottlieb, Lewiston.—p. 155.
Graduate Education in Medicine. F. T. Hill, Waterville.—p. 159.
Of Making Many Books. R. Bliss, Bluehill.—p. 162.

Michigan State Medical Society Journal, Lansing

39:373-452 (June) 1940

- Hygiene of Infants and Children. R. M. Smith, Boston.—p. 391.
Oesophagus Posterior: Incidence, Significance and Management. L. A. Calkins, Kansas City, Kan.—p. 396.
Arthritis: Acute Gonococcal and Gouty. R. H. Freyberg, C. J. Smyth, W. D. Block and W. S. Preston, Ann Arbor, Mich.—p. 402.
Lesions of Mouth. A. R. Woodburne, Detroit.—p. 407.
Biliary Tract Disease: Surgical Management. G. K. Glasgow and G. D. Livingston, Detroit.—p. 411.

Military Surgeon, Washington, D. C.

86:529-624 (June) 1940. Partial Index

- Naval Museum of Hygiene and Its Founder, Jerome Kidder, Surgeon, U. S. Navy. E. R. Stitt.—p. 529.
Peace Time Training to Meet Mobilization Needs. L. C. Fairbank.—p. 539.
Eosinophilia (Acidophilia) Bodies in Common Cold. H. H. Parsons.—p. 543.
Sulfapyridine Therapy in Pneumonia. H. P. Marvin, A. L. Bradford and W. H. Ketchum.—p. 554.
Long Distance Transportation of Wounded by Air at High Altitudes. H. Kowalzig.—p. 565.
Modern Anesthesia for War Surgery. G. E. Donaghy.—p. 577.
Causes of Failure in Physical Examination for Flying as Seen in Cadet Applicants. C. L. Leedham.—p. 583.
Vineet's Stomatitis. R. W. Leigh.—p. 588.
Hints About Marching Feet. H. Hansen.—p. 592.
March Foot. H. W. Meyerding and G. A. Pollock.—p. 593.
Postmobilization Chest Survey. W. C. Pollock.—p. 596.

Minnesota Medicine, St. Paul

23:383-458 (June) 1940

- Organized Medicine and Industrial Health. C. M. Peterson, Chicago.—p. 383.
Defense of Insanity in Criminal Cases. J. A. Garrity, Moorhead.—p. 387.
Extension of Group Hospital Service. A. M. Calvin, St. Paul.—p. 391.
Survey of Health Activities and Problems Among Former University Students. C. J. Potthoff and C. R. Pace, Minneapolis.—p. 397.
Eye Defects Causing Loss of Vision. W. H. Fink, Minneapolis.—p. 400.
Prenatal Care and Its Relation to Late Toxemias. A. G. Schulze, St. Paul.—p. 406.
Sulfathiazole in Otolaryngology. B. G. Levin, St. Paul.—p. 410.
*Significance of Inhalant Allergens in Treatment of Bronchial Asthma of the Child. A. V. Stoesser, Minneapolis.—p. 413.
Ewing's Tumor (Hemangio-Endothelioma: Endothelial Myeloma: Solitary Diffuse Endothelioma): Problem in Differential Diagnosis. H. W. Meyerding and G. A. Pollock, Rochester.—p. 416.
Rat Mite Dermatitis in Minnesota. W. A. Riley, Minneapolis.—p. 423.

Inhalant Allergens and Bronchial Asthma of Children.

—In a study of 329 children with bronchial asthma Stoesser found that, in 252 foods, inhalants and pollens were the causative factors. Fifty-eight children had attacks of asthma associated with infections of the upper part of the respiratory tract. Because tonsillitis occurred frequently in this group, the tonsils and adenoids were removed and thirty-eight obtained definite relief. The remaining twenty were not helped and a few of them were made worse by the operative procedures. The asthmatic attacks of ten children whose tonsils and adenoids had been removed many years before the attacks occurred were based on chronic infections of the respiratory system. Nine children failed to respond to any form of treatment except the use of potassium iodide. This preparation produced a more or less specific result. The inhalant group of allergens exclusive of the pollens was the cause of asthma among 122 children. House dust, feathers and cottonseed were the most important inhalants. Hyposensitization therapy for the inhalant allergy did not give encouraging results. The children sensitive to house dust were difficult to treat because this inhalant could be reduced but not completely removed from the environment. The cases sensitive to feathers responded well to the thorough removal of the inhalant. At first the children sensitive to cottonseed presented a difficult problem, but with the reduction or elimination of the lint dust from the environment good results were obtained. Some of the articles of furniture containing lint cotton were replaced by special mattresses and cushions

made of materials considered to be very weak allergens. The patients sensitive to animal emanations and some of the other inhalants were easily taken care of by more or less routine measures. The only exception was sensitivity to fish glue. The children sensitive to this allergen required hyposensitization therapy and the results were fairly good. Sudden changes in the weather did have some influence on the asthma, especially among children sensitive to house dust.

Missouri State Medical Assn. Journal, St. Louis

37:233-266 (June) 1940

- The Challenge Accepted. J. R. McVay, Kansas City.—p. 233.
The Responsibility of Medical Care. C. E. Burford, St. Louis.—p. 235.
Cerebral Syndrome. L. B. Alford, St. Louis.—p. 236.
Backache During Pregnancy and Its Management. E. Lissack, Concordia.—p. 238.
Hay Fever: Value of Daily Atmospheric Counts of Pollen Grains and Mold Spores in Diagnosis and Treatment. F. K. Hansel, St. Louis.—p. 241.
Allergy and Its Treatment. J. Backlar, Clayton.—p. 246.

Nebraska State Medical Journal, Lincoln

25:205-244 (June) 1940

- Organic Heart Disease (Clinic). S. A. Levine, Boston.—p. 209.
Surgical Diagnosis: Practical Concepts. R. H. Whitam, Lincoln.—p. 213.
Principles of Reconstruction in Ankle Malunion. W. R. Hamsa, Omaha.—p. 218.
Menus, Diets and Nutrition. M. J. Breuer, Lincoln.—p. 222.
Early Recognition of Suicidal Tendencies. H. A. Wigton, Omaha.—p. 226.
Prostatic Hypertrophy versus Neurogenic (Cord) Bladder: Differential Diagnosis. P. Adams, Omaha.—p. 229.
Urinary Calculi (Urolithiasis). C. W. Mason, Omaha.—p. 232.

New Jersey Medical Society Journal, Trenton

37:295-346 (June) 1940

- *Pulmonary Abscess: Report of Forty-one Cases. P. Geary, Plainfield.—p. 297.
Vasomotor Regulation of Temperatures of Extremities in Health and Disease. B. T. Horton, C. Sheard and Grace M. Roth, Rochester, Minn.—p. 311.
Duties of a President of a County Society. R. A. Schaaf, Newark.—p. 323.

Pulmonary Abscess.—Geary treated forty-one patients who had the nontuberculous type of pulmonary abscess. Twenty-eight were males and thirteen females. There were three cases in the first decade, five in the second, fourteen in the third, four in the fourth, eleven in the fifth and four in the sixth. Removal of the tonsils and adenoids was the procedure in 27 per cent. Next to aspiration in etiologic importance is pneumonia. The lesion is caused by an infected nidus with a surrounding inflammation and edema which eventually localizes. Subsequently liquefaction of the devitalized center is produced by saprophytic organisms. The various organisms (fusiform bacilli, spirilla, streptococci, staphylococci, fungi and the like) are those which normally exist in the mouth in a more or less dormant form. Pulmonary abscess is usually solitary. The patient complains of pain in the chest, chills, prostration, fever and often cough, which in the beginning is nonproductive. These symptoms continue with little change for from a few days to three weeks, when expectoration and severe cough begin. The breath is pungent. When expectoration of foul material begins, a large quantity of sputum may be expectorated over a short period indicating that the abscess has broken into a bronchus and the process of liquefaction is well established. Because the sputum is blood tinged and the symptoms differ from pneumonia, pulmonary tuberculosis is often suspected. However, foul sputum is rare in uncomplicated tuberculosis and the onset does not overwhelm the patient as quickly as the acute pulmonary abscess. A chronic pulmonary abscess would have a mortality of more than 90 per cent if it were left untreated. Aspiration through the chest wall should never be done. Since early treatment is desirable, the following conditions should suggest pulmonary abscess: (1) a pulmonary complication following any operation, delivery, operative manipulation, general anesthesia or localized infective process, (2) thick foul sputum, in the absence of a history of chronic bronchiectasis, and (3) foul sputum, coupled with x-ray evidence of a solitary abscess shown by a fluid level in which the whole lesion is circumscribed. The most important phase of treatment is prophylactic. Bronchoscopy is of great

value in removing secretion and in detecting and removing foreign bodies causing lung abscess and it may localize the site of the purulent secretion. Bronchoscopy, postural drainage, bed rest and other conservative measures are indicated in the early stages. If it is evident from roentgenograms taken at weekly intervals that the condition is stationary or getting worse, operative intervention should not be delayed even though the patient seems to be improving clinically. If a lesion is localized and improvement is doubtful after two or three weeks of conservative treatment, operative drainage is indicated. Doubt may exist for several months more, by which time the abscess becomes chronic and the operation is less likely to be successful and the convalescence prolonged. If the tissues are indurated and there is no motion between the pleural layers the procedure can be performed in one stage. If doubt exists, the operation is done in two stages, the wound packed with plain gauze and left wide open. The author used conservative measures in the treatment of seventeen patients with four deaths, or a mortality of 23 per cent. Twenty-four patients were operated on, six of whom died, giving a mortality of 25 per cent. The patients subjected to operation were more seriously ill than the others and had already had conservative therapy.

New York State Journal of Medicine, New York

40:909-982 (June 15) 1940

- Globin Insulin: Clinical Study. G. B. Andrews and W. A. Grant with assistance of Alice V. Wood and M. L. Jones, Syracuse.—p. 913.
Management of Varicose Veins in Private Practice. I. A. Brunstien, New York.—p. 918.
Practical Value of Endometrial Biopsies. D. R. Mishell, Newark, N. J., and L. Motyloff, New York.—p. 928.
Sectional Radiography in Diagnosis of Interesting Thoracic Problems. G. J. Plehn and R. B. Hoenig, New York.—p. 932.

Radiology, Syracuse, N. Y.

34:651-782 (June) 1940

- Roentgenologic Differential Diagnosis Between Cancer and Diverticulitis of Colon. R. Schatzki, Boston.—p. 651.
Hematologic Diagnosis and Roentgenologic Treatment of Myelogenous Leukemia. W. C. Popp and C. H. Watkins, Rochester, Minn.—p. 661.
Brief Observation on Erythrocyte Sedimentation in Relation to Irradiated Malignant Tumors. M. F. Madrazo, Mexico City, Mexico.—p. 668.
Fate of Cranial Defects Secondary to Fracture and Surgery: Follow-Up Study of 150 Patients. M. A. Glaser and E. S. Blaine, Los Angeles.—p. 671.
Duodenal Ulcer in Presence of Gallbladder Symptomatology. E. J. Ryan, New York.—p. 685.
Milliammeter Inaccuracy Caused by Control Cabinet. M. M. D. Williams, Rochester, Minn.—p. 691.
Congenital Cystic Malformation of Lungs, Formerly Known as "Vesicular" or "Hypertrophic Pulmonary Emphysema," Recently Described as "Congenital Cystic Disease of Lungs": Report of Case. C. T. Sharpe, New York.—p. 692.
*Cavitary Bronchogenic Carcinoma. H. Hauser and S. E. Wolpaw, Cleveland.—p. 698.
Primary Sarcoma of Stomach: Report of Three Cases. L. K. Chent, Oklahoma City.—p. 714.
Responses of Drosophila Pupae to X-Rays. P. S. Henshaw and I. M. Golomb, New York.—p. 721.
Roentgenographic Unsharpness of Shadow of a Moving Object: II. S. R. Warren Jr., Philadelphia.—p. 731.

Cavitary Bronchogenic Carcinoma.—According to Hauser and Wolpaw, cavitation occurs in all types of bronchogenic carcinoma but most frequently in the squamous cell variety. Fifteen instances of cavitation were demonstrated in an x-ray study of 127 cases of primary bronchogenic carcinoma admitted to Cleveland City Hospital from 1927 to 1937 inclusive. The diagnosis was proved by necropsy or by bronchoscopic or operative biopsy. The ages of the patients varied from 42 to 68 years. Their histories failed to reveal a clinical picture pathognomonic of a cavitary bronchogenic carcinoma. The important symptoms (cough, expectoration, weight loss and weakness) are also common to tuberculosis and lung abscess. Irregular fever above 99.5 F. was present at some time during the course of the illness of thirteen patients. Hemoptysis occurred in twelve and pain was present in ten. Five patients had clubbing of the fingers. The onset of the illness of the fifteen patients was insidious, with an irritative cough as the initial symptom. The cough was nonproductive in eight for from three to eight months. This latent period before expectoration ensues is of value in the differentiation from lung abscess, as patients with the latter lesion rarely remain sputum free for this length of time. In

contrast to pulmonary abscess, foul expectoration was observed in only two cases. Pain was common, appeared early, and was constant, severe and nonpleuritic in type. Such pain which fails to respond to medication is unusual in abscess and pulmonary tuberculosis and should suggest carcinoma. Decreased breath sounds and voice sounds in the involved area, indicating the presence of some degree of bronchial obstruction, were present. However, similar signs accompanied by rales and impairment of the percussion note may also occur in abscess and tuberculosis. Nevertheless, in the presence of x-ray evidence of cavitation, diminished or absent breath sounds should suggest an underlying carcinoma. Horner's syndrome, obstruction to mediastinal blood vessels, vocal cord paralysis, and lymph node and subcutaneous metastases are also suggestive. However, as cavitory bronchogenic carcinomas are usually of the squamous cell variety, extrathoracic metastases will not be frequent. At the time of admission to the hospital the patients presented a chronic, steadily progressive illness in its terminal stages. Eleven of them died within two months of admission. The total duration of life of ten from onset of symptoms was less than one year. One patient lived twenty months after the initial symptoms. X-ray signs in cavitory bronchogenic carcinoma include all features observed in other types of cancer of the bronchus, with the addition of cavitation. Signs of atelectasis are more often absent than present. The location of the tumor is variable. If extensive the cavity may involve more than one lobe, especially if it originates in the base of either upper lobe. The lesion is often difficult to demonstrate in the postero-anterior view, and lateral or oblique projection is often required. The average size of the cavity among the fifteen patients was 5.2 cm.; the smallest was 1.5 cm. and the largest 14 cm. Enlarged lymph nodes may be present in the hilus as a result of regional metastasis. The cavity simulates that found in pulmonary abscess and gangrene, tuberculosis or bronchiectasis. In the presence of a cavitory lesion of the lung, x-ray evidence of metastasis in the bones, brain or other soft tissues may aid in establishing the diagnosis. Bronchograms, by demonstrating filling defects or occlusion of the lumen of the bronchus leading to the cavity, will give the clue to the diagnosis of neoplasm.

Rhode Island Medical Journal, Providence

23:75-108 (June) 1940

- Gastroscopy and Clinical Medicine. R. S. Bray, Providence.—p. 75.
Brain Abscess with Brain Potentials. C. A. McDonald and M. Korb, Providence.—p. 81.
Causation of Postoperative Distention. W. P. Davis, Providence.—p. 85.
Diagnosis of Intestinal Obstruction. E. A. Shaw, Providence.—p. 87.
Treatment of Postoperative Distention. H. B. Moor, Providence.—p. 90.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

48:333-402 (June) 1940

- Vascular Lesions of the Extremities. P. G. Flothow, Seattle.—p. 333.
Vernix Caseosa: Manifestation of Vitamin A Deficiency: Preliminary Report. J. V. Straumfjord, Astoria, Ore.—p. 341.
Present Status of Vitamin K. C. P. Larson, Tacoma, Wash.—p. 352.
Cholecystoscopy Following Cholecystostomy: Report of Procedure and Twelve Cases. A. Laubersheimer, Los Angeles.—p. 357.

West Virginia Medical Journal, Charleston

36:241-288 (June) 1940

- Hypothyroidism. H. H. Golz, Clarksburg.—p. 241.
Diagnosis and Treatment of Atypical Lymphoblastoma. H. W. Jaeco, Pittsburgh.—p. 249.
Selection of Items for a Public Health Program. J. W. Mountin, Washington, D. C.—p. 253.
Granulocytopenia: Case Treated with Adenine Sulfate. F. J. Holroyd, Princeton.—p. 261.
Liver Function and Carbohydrate Metabolism. J. S. Pearson, Huntington.—p. 263.
New Viscera Retractor. H. C. Myers, Philippi.—p. 268.
Blood Smear in Diagnosis. W. L. Claiborne, Huntington.—p. 270.
Malignant Tumor of Kidney: Report of Case. T. J. McBee and C. C. Fenton, Morgantown.—p. 272.

Wisconsin Medical Journal, Madison

39:413-500 (June) 1940

- Low Back Pain: I. Anatomic Aspect. E. J. Carey, Milwaukee.—p. 427.
Id.: II. Medical Aspect. G. H. Coleman, Chicago.—p. 446.
Id.: III. Urologic Aspect. H. Culver, Chicago.—p. 450.
Id.: IV. Gynecologic Aspect. E. Cary, Chicago.—p. 456.
Id.: V. Orthopedic Aspect. E. W. Ryerson, Chicago.—p. 459.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

52:173-204 (June) 1940

- Pili Torti, with Discussion of Molecular Structure of Condition and Its Relationship to Monilethrix: Clinical Description, X-Ray and Optical Examination; Case. F. F. Hellier, W. T. Astbury and Florence O. Bell.—p. 173.
Sudden Death in Infantile Eczema. J. H. T. Davies.—p. 182.
Some Observations on Intracutaneous Reactions in Allergic Eczemas. H. Haxthausen.—p. 191.

British Medical Journal, London

1:879-918 (June 1) 1940

- Mass Radiography, with Special Reference to Screen Photography and Pulmonary Tuberculosis. F. J. Bentley and Z. A. Leitner.—p. 879.
Traumatic Extradural Hemorrhage. A. R. Short and Marjorie Dunster.—p. 884.
Peripheral Gangrene of Unknown Origin: Two Cases. R. Marshall.—p. 886.
Panic States in Civilians. H. Stalker.—p. 887.
Vitamin E and Habitual Abortion. A. L. Bacharach.—p. 890.

Edinburgh Medical Journal

47:369-440 (June) 1940

- *Thrush, with Special Reference to Vaginal Thrush. W. G. Liston and L. G. Cruickshank.—p. 369.
Pathology of Speech and Voice. D. Guthrie.—p. 391.
Use of Estrogens in Obstetrics and Gynecology. A. I. S. Macpherson.—p. 406.
Some Aspects of Malnutrition Problem. J. P. McGowan.—p. 425.

Vaginal Thrush.—Liston and Cruickshank found forty-nine out of 200 pregnant women with leukorrhea to be suffering from vaginal thrush. Next to trichomoniasis (40 per cent) vaginal thrush was the second most important cause of leukorrhea. This vaginal infection may be communicated to the babies and in some institutions it has given rise to severe epidemics associated with fatalities not always recognized as due to thrush but attributed to diarrhea, bronchitis and bronchopneumonia. The authors' examination of the patient consisted in interrogating the patient, inspecting the vulva and vagina, the making of films on slides for microscopic examination, washing out the vagina with sterile saline solution at a pH of 7 and collecting this in Liston's vaginal sampling pipet for the purpose of determining the pH of the vaginal contents and, roughly, the amount of glycogen present in the epithelial cells. The parasite can be recognized and the disease diagnosed by examining under a low power lens material obtained directly from the lesions in which microscopic portions of the septate pseudomycelium together with blastospores are found. The disease should be sought for and treated ante partum lest the baby become infected. The infection may be overlooked unless the parasite is sought. The symptoms in some cases may be trivial. The presence of the parasite in the vagina seems to depend on the pH reaction of the vaginal contents. The mean pH reading found on the examination of thirty-two of the cases was 4.8. The mean pH reading of twenty-seven normal pregnant women was 4.4 and of thirty-four pregnant women infected with *Trichomonas vaginalis* it was 5.5. The authors attach great importance to the pH reaction of the vaginal contents as a factor encouraging or inhibiting the development of vaginal thrush.

Journal of Endocrinology, London

2:1-140 (May) 1940. Partial Index

- Method of Assay for Progesterone Based on Inhibition of Uterine Estrus. A. J. Szarka.—p. 1.
Mechanism of Action of Gonadotropin from Pregnancy Urine. B. Zondek.—p. 12.
Morphologic Relationship Between Testicular Nerves and Leydig Cells in Man. H. Okkels and K. Sand.—p. 38.
Metabolism of Parent Compounds of Some Simpler Synthetic Estrogenic Hydrocarbons. S. W. Stroud.—p. 55.
Excretion of Free Estrogen During Uterine Bleeding. A. Palmer.—p. 70.
Isolation of Estrone from Ox Adrenals. D. Beall.—p. 81.
17-Ketosteroid, Androgen and Estrogen Excretion in Urine of Cases of Gonadal or Adrenal Cortical Deficiency. N. H. Callow, R. K. Callow and C. W. Emmens.—p. 88.
Rate of Loss of Activity of Antigonadotropic Serum in Vivo. M. R. A. Chance.—p. 99.
Excretion of Estrogen and Pregnandiol by Pregnant and Parturient Women: Normal and Toxemic Cases. A. M. Hain.—p. 104.

Journal of Laryngology and Otology, London

55:197-236 (April) 1940

Nasal Osteomas. A. S. Handousa.—p. 197.

Importance of Biologic and Endocrinologic Factors in Otorhinolaryngology: Report Delivered at the Annual Meeting of the Otolaryngologic Society in Odessa. A. Geschelin.—p. 212.

Journal of Pathology and Bacteriology, London

50:393-560 (May) 1940. Partial Index

Histology of Rat's Liver During Course of Carcinogenesis by Butter-Yellow (*p*-Dimethylaminoazobenzene). J. W. Orr.—p. 393.

Occurrence in Normal Mice of Pleuropneumonia-like Organisms Capable of Producing Pneumonia. D. G. f. Edward.—p. 409.

Chemotherapy of Experimental Staphylococcal Infection in Mice with Drugs of Sulfanilamide Group. P. Browning.—p. 431.

Passive Protection of Mice with Immune Horse Serum Against Living Staphylococci. L. N. Farrell and J. S. Kitching.—p. 439.

First Effects on Mouse Skin of Some Polycyclic Hydrocarbons. B. D. Pullinger.—p. 463.

Postmortem Glycolysis. J. L. Hamilton-Paterson and Elsie W. M. Johnson.—p. 473.

Bactericidal Action of Normal Serums. J. Gordon and K. I. Johnstone.—p. 483.

Endocarditis Due to a New Species of *Haemophilus*. O. Khairat.—p. 497.

*Cancer of Rectum: Analysis of 1,000 Cases. C. E. Dukes.—p. 527.

Cancer of Rectum.—According to Dukes, of 1,000 patients with rectal cancer removed by radical excision there were 650 men and 350 women. These figures correspond to those reported by the registrar general for 1936, 3,303 deaths in males and 2,083 in females, giving a ratio per thousand of 613:387. The mean age of the 350 women was 55.1 and of the 650 men 58.6. The earlier age of onset in women is also brought out by the fact that 11.2 per cent of the women were less than 40 years of age as compared with only 6 per cent of the men. A similar difference is found in the registrar general's figures for England and Wales. A more widespread extension of the disease is likely to be found in young patients. In patients less than 40 years of age, lymphatic metastases were found in 71.8 ± 4.3 per cent, whereas in the group from 40 to 59 years of age they were found only in 50.9 ± 2.4 per cent. This relation of spread and the age of the patient held for both sexes. This might be attributed to delay in receiving surgical treatment or to a more rapid progress of the disease in young patients. The latter appears to be the most likely explanation. At the time of surgical treatment most rectal cancers are oval, extend over two or three quadrants of the rectum and measure from 2 to 3 inches in diameter from above downward. High grade malignant tumors were most frequent in young patients. In about 15 per cent of cases of rectal cancer regarded as operable the growth was still restricted to the rectal wall, in about 35 per cent it had spread by direct continuity into the perirectal fat but had not yet caused lymphatic metastases and in 50 per cent lymphatic metastases were found. Extension of rectal cancer within the lumen of the hemorrhoidal veins was found in approximately 18 per cent of the operative specimens. Usually one malignant growth was found, but associated malignant tumors were fairly common and they may be encountered in multiple primary cancer, secondary malignant tumors and familial intestinal polyposis. Evidence of lymphatic permeation was found in 4.4 ± 3 per cent of grade 1 tumors, 8.6 ± 5.1 per cent in grade 2, 30.1 ± 4.2 per cent in grade 3 and 50 ± 15.8 per cent in grade 4. The respective venous spread was 4.4 ± 3 , 12.2 ± 1.8 , 36.3 ± 4.5 and in 20 ± 12.7 per cent. These considerations emphasize the importance of the microscopic structure of rectal cancer, since this may allow an estimate to be made of its rate of growth and may even provide an indication of the extent of local, lymphatic or venous spread. In its earliest stage rectal cancer takes the form of a small thickening of the mucous membrane or a hard nodule in a preexisting adenoma or villous papilloma. As the growth increases it gives rise to ulceration. Ulceration usually commences when the growth has spread through the submucosa into the muscle. Deep ulceration indicates that the growth has spread through the muscle into the perirectal tissues. All regions of the rectum may be affected approximately to the same extent, though probably the incidence decreases slightly on passing from the anus toward the pelvic colon.

Journal of Physiology, Cambridge

98:141-262 (May) 1940. Partial Index

Permeability of Blood-Aqueous Humor Barrier to Potassium, Sodium and Chloride in Surviving Eye. H. Davson and J. P. Quilliam.—p. 141.

Transmission of Light by Eye Media. K. J. W. Craik.—p. 179.

Effect of Mono-Iodoacetic Acid on Absorption of Water from Glucose Solutions in Subarachnoid Space. T. H. B. Bedford.—p. 185.

Determination of Metabolic Rate of Alcohol. M. Grace Eggleston.—p. 228.

Some Factors Affecting Metabolic Rate of Alcohol. M. Grace Eggleston.—p. 239.

Results of Adrenalectomy in Pregnant Albino Rat. T. McKeown and W. R. Spurrell.—p. 255.

Lancet, London

1:993-1034 (June 1) 1940

Death in the First Month and the First Year. C. McNeil.—p. 993.

Interstitial Emphysema and Pneumothorax After Operations on Neck. H. J. Barrie.—p. 996.

Antiserum and Sulfapyridine in Meningococcal Infections in Mice. C. R. Amies.—p. 999.

Atropine and Ergotoxin as Antidotes to Scorpion Toxin. A. Hassan and A. Hassan Mohammed.—p. 1001.

Autograph of Amputated Digit: Suggested Operation. H. Gillies.—p. 1002.

Concussional and Postconcussional Syndromes. C. T. van Valkenburg.—p. 1003.

Radiologic Demonstration of Adenoids. G. T. Calthrop.—p. 1005.

Purpura Haemorrhagica After Arsenic Therapy Treated with Vitamin P. D. R. Gorrie.—p. 1005.

1:1035-1070 (June 8) 1940

Pulmonary Tuberculosis: Diagnosis and Some Aspects of Treatment. F. G. Chandler.—p. 1035.

Aneurysm of Thoracic Aorta Treated by Wiring with Colt's Apparatus. R. S. Johnson.—p. 1037.

*Sulfathiazole in Bubonic Plague. S. S. Sokhey and B. B. Dikshit.—p. 1040.

Time Relations of Heparin Action on Blood Clotting and Platelet Agglutination. D. Y. Solandt and C. H. Best.—p. 1042.

Pathologic Fracture of Mandible: Nonunion Treated with Pedicled Bone Graft. P. P. Cole.—p. 1044.

Missed Abortion and Missed Labor. T. N. A. Jeffcoate.—p. 1045.

Radium and Radon: Biologic Reactions Compared. S. Russ and G. M. Scott.—p. 1048.

Sulfathiazole in Bubonic Plague.—Sokhey and Dikshit found sulfathiazole to be effective for plague in mice. Sulfapyridine also had some action. In human cases of plague the most important factor which decides the issue is the development of septicemia. Septicemia develops in mice from forty-eight to seventy-two hours after the induction of infection by the subcutaneous route. Therefore the authors started the administration of the drug at four different stages of the infection: at the time the infecting injection was given and twenty-four, forty-eight and seventy-two hours later. Twenty animals were used in each experiment. The mice were observed for at least thirty-one days. Plague organisms were never found in the organ smears and blood cultures of animals dying during the period of administration of the drug, but they were found in animals dying after the drug had been stopped, the only exception being in the experiments in which sulfapyridine was given in 10 mg. doses once a day for ten days. In this case some animals which died during the period of administration of the drug showed the presence of plague organisms. In human plague spontaneous recovery invariably results if the lymph glands prevent the spread of infection to the blood stream and the infection remains localized. The occurrence of such cases in different outbreaks is from 20 to 50 per cent. If the organisms pass the lymph glands and a septicemia results, death invariably follows unless an effective agent can be given to control the infection. The effective agent must be given before extensive destruction of the tissues of the organs has resulted. When the mice were given the drug before septicemia had set in, that is before forty-eight hours after infection, as little as 10 mg. of sulfathiazole twice a day for ten days saved nearly 80 per cent of the infected animals, and even better results were obtained by doubling this dose. Sulfapyridine produced about the same action as sulfathiazole in the early stages of infection with doses of the same order. When the administration of the drugs was started after septicemia had set in, a dose of 20 mg. of sulfathiazole twice a day for ten days cured approximately 80 per cent of infected animals when the drug was given forty-eight hours after infection and 65 per cent when given seventy-two hours after infection. Doubling this dose produced even better results, the survivals becoming 90 and 80 per cent, respec-

tively. These results are as good as those obtained with the Haffkine Institute antiplague serum. It is in this group of animals that sulfathiazole shows much more definite curative action than sulfapyridine. With the largest dose employed (40 mg. twice a day for ten days), when treatment was started forty-eight hours after infection, sulfathiazole cured 90 per cent of infected animals, whereas sulfapyridine cured only 10 per cent. Similar results were obtained when treatment was started seventy-two hours after infection. Since plague is much more severe in the mouse than in man, it is hoped that sulfathiazole will prove even more effective in human infection.

Practitioner, London

144:549-644 (June) 1940

- Diagnosis and Treatment of Fractures and Dislocations of Pelvis and Hip Joint. T. P. McMurray.—p. 549.
Common Fractures and Dislocations of Knee and Long Bones of Lower Limb. A. Perry.—p. 559.
Fracture Dislocations of Ankle Joint. R. Broomhead.—p. 571.
Common Fractures and Dislocations of Clavicle and Shoulder Joint. M. G. O'Malley.—p. 579.
Fractures and Dislocations at Elbow. A. Rocyn-Jones.—p. 589.
Fractures and Dislocations of Wrist and Hand. E. L. Farquharson.—p. 598.
Chest Injuries in Modern Warfare. T. H. Sellors.—p. 609.
Some Clinical Problems in Relation to Hemoptysis. P. Ellman.—p. 620.
Modern Therapeutics: XII. Drugs Affecting Control of Vasomotor System. K. D. Wilkinson.—p. 628.

Ginecologia, Turin

6:251-320 (May) 1940. Partial Index

- *Subcutaneous and Mediastinal Emphysema in Delivery. G. Nicora.—p. 297.
Strangulated Congenital Inguinal Hernia Containing Ovary of Infant Two Months Old. C. Matassi.—p. 316.

Subcutaneous and Mediastinal Emphysema in Delivery.

—Nicora reports an unusual case of subcutaneous emphysema of the left side of the neck and face developing in the course of a spontaneous delivery in a syphilitic patient 19 years of age. There was a delayed period of expulsion despite energetic contractions. The placenta was expelled ten minutes after the delivery of a living normal child. The placenta was normal but the umbilical cord was short (38 cm.). Emphysema reached its maximum one hour after the delivery. It remained stationary for the first few days of the normal puerperium and disappeared completely in the course of the next two weeks. There were no subjective symptoms. Roentgenograms of the thorax taken in the anteroposterior and oblique diameters on the third day revealed a subpleural emphysema at the point at which there were shadows of pleuropericardial adhesions. It was possible to follow the path taken by the air in the course of the formation of subpleural, mediastinal and subcutaneous emphysema. Roentgenograms taken on the fifteenth day were normal. The author believes that prolonged labor was caused by the short umbilical cord. The heightened respiratory pressure in the course of the expulsive period, in the presence of increased contractions of the abdominal muscles and diminished elasticity of the lung parenchyma caused by syphilis, were the probable causes of the production of minute lacerations in the pulmonary parenchyma, with consequent formation of subpleural, mediastinal and subcutaneous emphysema.

Deutsche medizinische Wochenschrift, Leipzig

66:589-616 (May 31) 1940. Partial Index

- *Thymus as Incretory Organ. C. Bomskov and L. Sladović.—p. 589.
*Hyperfunction of Thymus as Disease. E. Rehn.—p. 594.
Surgical Tasks in First Aid Station for Air Raids. A. W. Fischer.—p. 597.
First Attack of Malaria Tropica. L. Stutz.—p. 601.
Results of First Group Examinations in Four Industrial Regions. E. Zapel.—p. 601.

Thymus as Incretory Organ.—Bomskov and Sladović discuss investigations on the relationship between the thymus and the anterior lobe of the hypophysis. They obtained from the anterior lobe of the hypophysis of whales and of cattle forty different fractions and assayed them biologically on guinea pigs, rats and pigeons for the five known hormones of the anterior pituitary, namely the thyrotropic, the gonadotropic and lactotropic hormone, the growth hormone and the diabetogenic hormone. They were able to corroborate the results of other investigators with regard to the first four in proving them inde-

pendent entities. They failed to differentiate the growth hormone from the diabetogenic hormone and concluded that the two are identical. They investigated the question of whether the growth or the diabetogenic action of the hypophysis is exerted directly or through the intervention of another incretory gland. They were able to prove that it is a "tropic" hormone, that is, one which acts by way of affecting another gland, in this case the thymus. The authors point out that all "tropic" hormones of the hypophysis are protein bodies but that nearly all the hormones formed in the organs that are under the hormonal control of the hypophysis are not proteins but sterols (estrogen, progesterone, testosterone, corticosterone and so on). For this reason they experimented with a lipid extract from calf thymus and found that the thymus hormone is in the oil fraction of the thymus. The discovery of the thymus hormone made it possible to study the action of thymus in animal experiment. It was found that the thymus hormone increases growth, produces lymphocytosis, inhibits the development of the gonads and reduces the hepatic glycogen. All these functions are characteristic for the infantile organism. The thymus of young animals was found to contain larger quantities of hormone than that of full grown animals. The thymus hormone differs from other hormones in that it does not occur free in the blood serum but is carried in the lymphocytes. The discovery of the thymus hormone has thrown light on such clinical entities as exophthalmic goiter, status thymicolymphaticus and thymus death. Animal experiments demonstrated that the thymus hormone inhibits the action of the thyrotropic hormone of the anterior hypophysis and that neither the thymotropic hormone nor the thymus hormone acts on the normal basal metabolism. Effects which could be produced experimentally with the thymus hormone, namely growth, lymphocytosis and inhibition of the development of the gonads, are also observed in status thymicolymphaticus. Thymus death is an acute heart death, the result of glycogen deficiency of the cardiac muscle. Even small quantities of thymus hormone or of thymotropic hormone produce an extreme reduction in the glycogen content of the heart. In order to determine the involvement of the thymus in other diseases, the authors developed a method which detects in the urine not only thymotropic but also thymus hormone. The predominant effect of both hormones is the mobilization of the carbohydrates. This mobilization differs from that effected by the thyroid in that it produces growth, whereas that of the thyroid produces energy.

Hyperfunction of Thymus as Disease.—According to Rehn, thymus hormone, which during childhood and youth supports growth and is responsible for cell regeneration in adults, may lead to disease and death if its production is unchecked. The mobilization of glycogen from the liver necessary for growth produces, if it goes beyond this need, the diabetes of childhood and complete depletion of glycogen of the liver and heart. The gonads, chief antagonists of the thymus, do not as yet function in childhood and this explains the unchecked course of status thymicolymphaticus in childhood. Periods of hormonal tension before, during and after puberty will lead to thymic disturbances more frequently than will other periods. The author suggests that hyperfunction of the thymus during puberty is responsible for acromegaly and eunuchoidism. That hyperfunction of the thymus plays a part in exophthalmic goiter is proved by the frequent detection of an enlarged thymus in the presence of postoperative heart failure in these patients. The activity of the thymus becomes evident by the elimination of the thymus hormone in the urine, which can be detected by a method devised by Bomskov. The author investigated the function of the thymus in ten cases of exophthalmic goiter. In some the thyroid hormone may produce a secondary hyperfunction of the thymus. If early administration of iodine calms the thyroid in such cases, the irritation and hyperfunction of the thymus disappear. In other cases of exophthalmic goiter the hyperfunction of the thymus dominates the clinical picture. The treatment here must consider the thymus. The author thinks that myasthenia associated with exophthalmic goiter is the result of thymic hyperfunction. Involvement of the thymus should be searched for in every case of exophthalmic goiter. Since the lymphatic system has an important part in the transmission of thymic secretion, it seemed logical to investigate the behavior of the

thymus in one of its most serious disorders, Hodgkin's disease. A severe if not exclusive involvement of the thymus in Hodgkin's disease is manifested by the extreme thymic hyperfunction, by the tremendous amount of hormone which produces a strong lymphatic stimulus and results in blastoma-like foci, by the frequent development of Hodgkin's disease following hormonal tension of puberty, and by the favorable effect of mediastinal irradiations which in reality are irradiations of the thymus. The smallest dose of thymus hormone administered to healthy subjects produces within a few days a pronounced leukocytosis or lymphocytosis. Treatment of hyperfunction of the thymus must aim at a decrease of the functional activity of the organ. The oldest method is surgical reduction, first carried out by Rhcn in 1906. Resection of the thymus is advocated for tumor or tumor-like enlargement of the thymus. In cases in which the operation seems too dangerous, roentgen irradiation is preferable. The extreme ray sensitivity of the thymus facilitates this type of treatment but also demands caution, because dysfunction is likewise dangerous.

Wiener klinische Wochenschrift, Vienna

53:415-434 (May 24) 1940

Dietetic Treatment of Dysentery. F. Hamburger.—p. 415.

*Bacteriology, Serology, Pathologic Anatomy and Epidemiology of Dysentery. T. Korschegg.—p. 415.

Myeloblastic Reaction in Atypical Tuberculosis (Avian Tuberculosis). R. Stöger.—p. 419.

Rare Infectious Dermatoses. S. Wolfram.—p. 424.

Bacillary Dysentery.—According to Korschegg, four types of dysentery bacilli can be differentiated serologically: (1) Shiga-Kruse, (2) Kruse-Sonne, (3) Schmitz and (4) the Flexner group, which includes the Flexner, Y and Strong types. The organisms differ likewise with regard to the formation of toxins. The author believes that it is better to speak of severely toxic and mildly toxic than of true and pseudo dysentery bacilli. The morphologic aspects of dysentery do not permit the identification of the type of the bacilli. In some epidemics only one organism was isolated, whereas in others several were encountered. Several organisms have been found in the same patient. Such mixed infections presumably cause especially severe forms. In the course of an epidemic during the Polish war only the Shiga-Kruse bacillus was observed at first, but later the Y and the Flexner types were detected. The author suggests that the most common port of entry is the mouth. The disease is localized chiefly in the large intestine; involvement of the small intestine occurs only in severe cases. In the early stage there exists a catarrh of the mucosa. After a few days or a week the mucosa becomes necrotic. Ulcerations appear during the second or third week, never before the end of the first. They are always present in large numbers and are usually most profuse in the sigmoid and the rectum; they have a tendency to coalesce. Healing cannot be expected before the end of the third week. In some cases new attacks occur before the healing is complete and subchronic or chronic dysentery develops. The most severe but fortunately rare complication of dysentery is intestinal perforation. The articular complications are of the nature of a serous arthritis, occasionally with severe involvement of the bursae. Hepatic abscesses are rare. If death ensues it is usually the result of exhaustion. It is difficult to determine the source of infection in sporadic cases but there is evidence that carriers are responsible. Such carriers may also give rise to epidemics. Dissemination by contaminated food or water is not so important in dysentery as in cholera or typhoid. Epidemics have been caused by contaminated milk or other foods, but such epidemics are the exception. As a rule epidemics are produced by direct contact or by contact through soiled linen, clothing and eating utensils. The dissemination in localities often begins with family or house epidemics which become street and finally town epidemics. Large epidemics occur most frequently during summer and early fall and are more frequent among rural than among urban population. From these and other observations it has been assumed that flies are instrumental in dissemination. Investigations on this problem disclosed that flies which had been in contact with the excreta of dysentery patients harbored dysentery bacilli many hours after such contact. The author emphasizes the great importance of dysentery during war.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

84:1681-1788 (May 4) 1940. Partial Index

Burns of Throat. E. Huizinga.—p. 1682.

*Hypertrophic Pyloric Stenosis in Adults. J. F. Nuboer.—p. 1687.

*Pancreatic Lithiasis. J. K. Kraan and L. Meyler.—p. 1695.

Polyclical Psychotherapy. A. H. Fortanier.—p. 1702.

Hypertrophic Pyloric Stenosis in Adults.—Nuboer discusses two adults with pyloric stenosis. The first patient, a woman aged 30, had a history of four years of gastric disturbances. The symptoms and the examination suggested stenosis of the pylorus. At operation a muscular pyloric stenosis and gastritis were found. The second patient, a man aged 36, had a history of frequent attacks of vomiting since childhood and typical ulcer symptoms for the last four years. Clinical examination indicated an ulcer on the small curvature of the stomach, but x-ray examination did not clearly reveal an anomaly of the pylorus. At laparotomy the small curvature seemed shortened and an infiltration was found; the pylorus could be felt as a firm ring. Polya's ventricular resection was done and recovery was uneventful. Microscopic examination of the surgical specimen revealed two small old ulcers on the lesser curvature, chronic erosive gastritis and muscular hypertrophy of the pylorus. The author reviews the literature and emphasizes that the anatomic aspect of pyloric stenosis in adults greatly resembles that seen in nurslings. This fact, and the observation that in adults with pyloric stenosis the history of gastric disturbances often goes back to early childhood, seem to indicate that the pyloric stenosis of adults is a continuation and exacerbation of a congenital defect. Gastric resection is advocated as the best treatment for this condition in adults.

Pancreatic Lithiasis.—Kraan and Meyler report the history of a man who presented symptoms of diabetes mellitus and of nontropical sprue. The disturbances in the sugar metabolism indicated an impairment in the internal secretion of the pancreas. Steatorrhea and other abnormal products of digestion in the feces, the lack of pancreatic ferments in the duodenal juice and the reduction of diastase in the feces, blood and urine indicated a disturbance in the external pancreatic secretion. An x-ray examination of the kidney made because of tenesmus and painful micturition failed to disclose renal or ureteral calculi. A large number of calcium spots were detected in the region of the pancreas. The disorder was diagnosed as pancreatic lithiasis. The literature contains a number of reports on calcification of the pancreas. The symptoms on which the diagnosis is based are (1) pain in the upper part of the abdomen, which is constant and indefinite but may also be colic-like; (2) disturbances in the external pancreatic secretion with resulting diarrhea, emaciation, abnormal feces and deficiency of ferments in the duodenal juice; (3) diabetic symptoms and hypoglycemia; (4) roentgenologic signs. Intermittent hypoglycemia is particularly characteristic of pancreatic lithiasis.

Ugeskrift for Læger, Copenhagen

102:467-496 (May 9) 1940

*Hematogenic Changes in Ileitis, Especially Megalocytic Forms of Anemia. P. Plum and E. Warburg.—p. 467.

Studies on Effect of Diuretics Containing Mercury in Edematous Patients with Special Regard to Water and Chloride Content of Blood: Preliminary Report. A. Petersen.—p. 476.

Ten Cases of Exophthalmic Goiter Treated Operatively. E. Rosen.—p. 481.

Nocturnal Enuresis and Its Treatment. C. N. S. Gundtoft.—p. 483.

Hematogenic Changes in Ileitis.—Plum and Warburg report four cases of regional ileitis characterized by anemia as the prominent symptom. In the three with hyperchromic anemia the hydrochloric acid secretion of the stomach was not affected. Two of the patients had psychic disturbances. The authors suggest that psychic anomalies may depend on the intestinal disorder and the disturbance in resorption. Their cases seem to show that deficiency symptoms are not uncommon in inflammation of the small intestine and that in atypical anemia, perhaps also in pernicious anemia, attention should be directed to the intestine, especially the small intestine. Since definite improvement resulted from treatment with liver in two of the cases of hyperchromic anemia and has been maintained, they think that some of the regional changes in the ileum may be secondary to a deficiency disease.

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THE FUNCTIONAL POINT OF VIEW IN RHINOLOGY

CHAIRMAN'S ADDRESS

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ST. LOUIS

When a man sets out to tinker with an alarm clock one of two things is almost certain to happen: Either he gets it going or he has enough parts left over to make a wrist watch, and neither of them runs or ever will. The result does not depend on his virtuosity with a screwdriver nor does it rest on his knowledge of radio, firearms or locomotives. If he succeeds in putting it in order it is only because he understands how clocks work.

So it is with the nose. To deal successfully with a nose the rhinologist must understand the basic principles of surgery, to be sure. Granted he must be skilful with his hands. He must be conversant with the local anatomy. But above all he must know how a nose works.

Until recently he has unexplainably paid little attention to function. Many a monograph and many a textbook have been written on the nose with never a word about its physiology. Many an operation has failed of its purpose because the surgeon had not clearly in mind how or even whether it might accomplish what he intended it to.

The reason for his long protracted indifference is not clear. Most of what he knew—or thought he knew—about nasal physiology had been discovered by some one not vitally interested in the nose. It was often the by-product of an investigation far removed from the problems of rhinology. It was not infrequently deduced from the observations of zoologists working with tissues not human but from animals whose habitats, environments and genealogies are wholly unlike our own.

Any one who attempts to prepare a course of lectures to advanced students on the physiology of the nose cannot fail to be dismayed at the scarcity of material available. From the indexes he may gather many titles scattered through the literature of the past fifty years, but he will be disappointed in the sum total of factual information.

Whether this is the cause or the effect of a widespread preoccupation with other problems on the part of our immediate predecessors is of no great moment. The fact remains that the authors of all but a very few textbooks have contented themselves with the mere mention of matters physiologic—usually a few introductory paragraphs, lost among the descriptions of head mirrors and office equipment—and then have proceeded,

with never a backward glance, to describe and endorse procedures which plainly showed that they still regarded the nose as only a distressingly tortuous air passage and nothing more. This misconception led to much futile therapy.

It resulted, for example, in the failure to differentiate surgically between a sinus empyema and an abscess. Even contemporary textbooks seldom point out that a pus filled nasal accessory cavity is essentially a space. an air cell, of proportions and relations important to its health, with sensitive functioning mechanisms, while an abscess is not a space at all but a collection of pus, rending tissues apart and creating, only after its evacuation, a cavity where no cavity has any business to be. To regard these two surgically as one and the same thing is a blunder responsible for much lingering distress.

It resulted further in a disregard for nasal tissues as such. Not so long ago it was widely taught that no special requirement was met by conserving them, that they could be sacrificed fairly promiscuously, merely for the surgeon's momentary convenience. No mention was made of air currents thus misdirected against some sensitive area of the upper nose, producing intractable headaches. Subsequent crusting was attributed not to the resulting dryness but to incomplete eradication, and more and more was done—instead of less and less—for the point of view was structural instead of functional.

These things are of the past—just barely. Ten years ago, before one of the national societies then meeting in San Francisco, I called a speculum a spade and inveighed against our indifference to the intimate workings of the nose.

Today my tirade would lack point. I am happy to say that the recrudescence of interest in nasal physiology has been due largely to the investigations of Americans. There have been repercussions in England, in Germany and particularly in the North Countries. It is encouraging that a purely physiologic subject was at last selected for official discussion by the fourth International Congress of Otolaryngology, to have been held next month in Amsterdam but now regrettably postponed. It is notable that the new work has, for the first time, come almost exclusively from the laboratories of rhinologists actively engaged in clinical work. On the whole it is based on experimental evidence of a quality which entitles it to our respectful attention.

It is the part of the clinician to apply such available knowledge intelligently to the individual case and to avoid routines which in industry may be the index of efficiency and production but in science are the graveyards of progress.

The application of new knowledge is twofold: To heed what has been done in the laboratory and to apply it wisely to the patient; to adopt new methods, new drugs, new operations intelligently is progress. It is likewise progress, though it seldom occurs to us, to

abandon old methods, old drugs and old operations when they have been discredited. Not to abandon them after they have been proved harmful is reprehensible.

One is constantly confronted with the need of a critical evaluation of methods. I shall not enlarge on this, as the therapeutic "how" and "why" will presently be threshed out on this floor. I wish only to point out that the functions of the nose, whatever they may ultimately prove to be, have a vital influence on the air we breathe. What could be more important?

I wish to add that it is not enough to maintain breathing channels but that the mechanisms by which the nose keeps itself clean must be conserved or restored if it is to continue functioning and maintain its possessor in comfort. It is not enough to know that quantities of moisture are required to saturate inspired air unless we act on that knowledge by conserving and cultivating the humidifying equipment of the mucosa, already often taxed to the limit by the droughts of central heating. It is not enough to know that air currents are evenly distributed over the streamlined contours of the nasal fossae without being keenly aware that they may not be misdirected with impunity. I will not labor the point.

Little by little, as the physiology of the nose is better understood, therapeutic and surgical methods will conform to it; but in the meantime it behooves us individually to find out more about how our alarm clock works before we begin throwing away any of the wheels.

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USE OF BISMUTH INJECTIONS TO MANAGE COURSE OF THERA- PEUTIC MALARIA

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Malaria is being used more and more in the treatment of resistant syphilis of the central nervous system as well as of dementia paralytica. This form of fever treatment has established its value in spite of the definite risk associated with it, even in selected cases. For this reason there is a growing need for some means of management of therapeutic malaria. Thus, if some agent were at hand to cause a temporary interruption in the course of the fever for even forty-eight hours, there would be an opportunity for the patient to recover from the effects of the fever. The cycle might then be allowed to continue until sufficient hours of hyperpyrexia had been accomplished.

In 1937 Fong¹ reviewed the literature on malaria mortality and reported eleven series of cases, totaling 13,267 patients. In this group, in part unselected, the mortality was 7.51 per cent. The usual causes of death

were physical exhaustion, kidney and liver insufficiency, and vascular collapse. With the exception of the last condition, death was as a rule not sudden; usually ultimate failure was heralded in ample time so that some form of supportive measure (malaria management) could have been used had it been available. It is for these untoward reactions in the course of malaria therapy that the use of thio-bismol is offered.

USE OF HEAVY METALS IN THE TREATMENT OF MALARIA

The value of preparations of bismuth and other heavy metals in the treatment of epidemic malaria has been mentioned by various writers. Speranza² has reported on the use of bismuth; Sanyal³ and deNunno⁴ have spoken of the value of antimony in treating quinine-resistant malaria; Gualdi⁵ has observed the action of gold, and Ross,⁶ Liu,⁷ deMello and Vernencar,⁸ Peroni⁹ and Bird¹⁰ have used mercury in combating the disease. Various arsenical preparations have been employed by Goldman,¹¹ Cleveland and Turvey,¹² Young and McLendon,¹³ Solomon, Epstein and Berk,¹⁴ Tardres,¹⁵ Sinton,¹⁶ Murphey¹⁷ and many others.

In May 1938 one of us¹⁸ reported the effect of thio-bismol (bismuth sodium thioglycollate) in twenty-one cases of malaria at Cleveland City Hospital. Of this series nineteen were an artificial asexual strain (used in the treatment of central nervous system syphilis) and two were naturally acquired tertian malaria. Since this original report, 129 patients from the Dermatology and Syphilology Services of City and of the University Hospitals have been studied. This included some 150 observations on bismuth and other heavy metals. Each patient had received an intravenous inoculation of malarial blood (from 2 to 5 cc. with no attempt as to type compatibility) and had every evidence of the disease. This strain has been kept alive for sixteen

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16. Sinton, J. A.: Parosan (Arsenic Preparation) and Dimeplasmin, *Indian J. M. Research* **17**: 815-820 (Jan.) 1930.

17. Murphey, E. E.: Use of Sodium Cacodylate in Malaria, *J. M. A. Georgia* **16**: 20-24 (Jan.) 1927; Sodium Cacodylate in Pernicious Malaria, *South. M. J.* **22**: 363-366 (April) 1929.

18. Schwartz, W. F.: Effect of Thio-Bismol on Therapeutic Malaria, *J. Pharmacol. & Exptl. Therap.* **65**: 175-184 (Feb.) 1939.

Read before the Section on Dermatology and Syphilology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

From the Department of Dermatology and Syphilology, Cleveland City Hospital, the University Hospitals, and Western Reserve University Medical School.

1. Fong, T. C. C.: Study of Mortality Rate and Complications Following Therapeutic Malaria, *South. M. J.* **30**: 1084-1088 (Nov.) 1937.

years by transinoculation from patient to patient and has lost none of its original vigor. Of this number 103 patients were given thio-bismol to manage the course of the therapeutic fever, and in addition to other soluble and insoluble bismuth preparations various compounds of antimony, mercury, arsenic and gold were employed. Further, sodium thioglycollate,¹⁹ the vehicle of thio-bismol (bismuth sodium thioglycollate) was tried to determine whether it played a part. This was done in order to make sure that it was the bismuth rather than the thioglycollate that had the antimalarial effect. In the process a few related heavy metals were only casually examined.

Antimony.—Fuadin, a brand of stibophen (sodium antimony biscatechol disulfonate of sodium), antimony and potassium tartrate and sodium antimony thioglycollate were employed.

Fuadin.—Only five patients were in this group. Doses of 1.5 and 2 cc. were ineffective, so a larger dose was tried. The results in all cases were uniform, so description of one typical reaction will suffice. The patient had excellent elevations every forty-eight hours. After the fourth chill, 3 cc. of fuadin was given intramuscularly and an additional 3 cc. was given intravenously. The malaria terminated and the patient was then carried on typhoid injections as a substitute. He was in the hospital for twenty-five days without a single spontaneous rise of temperature. On two occasions rare plasmodia were found in the peripheral blood after injection of epinephrine.

Antimony and Potassium Tartrate.—Observations were made on but two patients. One patient was given 0.05 Gm. in a 1 per cent solution intravenously before the seventh paroxysm was anticipated (this elevation came unaltered 40.7 C., or 105.3 F.) and 0.075 Gm. of the drug was given just before the eighth chill. This chill was reduced to 40 C. (104 F.) and no further paroxysms followed. Frequent blood examinations were made for parasites and only after injection of epinephrine (1 cc. subcutaneously) were any parasites found in eight days of observation. The second case was similar to this one.

Sodium Antimony Thioglycollate.—Two patients who were chilling were given 20 cc. of a 0.4 per cent solution intravenously. In each the chills were terminated, one for four days and one for five days, after which the cycle was resumed.

Extended study of antimony compounds may reveal a preparation suited to temporary checking of a therapeutic malaria course. The ones examined either stopped it entirely or had an effect unsuitable for our purpose.

Arsenic.—Arsphenamine, neoarsphenamine and mapharsen have been used for years either as a means of "slowing" the course of malaria or in combination with quinine in the attempt to terminate the fever when that drug alone has failed. There is no doubt that they have an antimalarial effect. However, it is not a reliable method of producing a "rest period" from the chills, since often a single injection fails to produce the desired result, or it may terminate the course of the fever entirely. Recent observations in additional cases were consistent with former experience and with the experience of others.

Mercury.—Salyrgan was used on three patients. Three injections of 2 cc. each were given on alternate days without any change in the subsequent course of the fever. Parasites were found in the blood stream without difficulty.

With mercuric succinimide, one patient was given 0.01 Gm. every day for ten days during the course of malaria without any alteration in the type of cycle or in the intensity of paroxysms. To another patient through error was exhibited 0.012 Gm. every six hours for five injections without any change.

Gold.—Gold sodium thiosulfate was used on two patients, the first receiving 10 mg. intravenously and the second 25 mg., without any effect.

Sodium Thioglycollate.—This preparation is the vehicle in which thiobismol is given, and it was administered to seven patients in doses exceeding that found in the usual injection of thio-bismol. There was no effect, even after long observation periods. Evidently the thioglycollate radical does not play a main role in the effect of thio-bismol on therapeutic malaria.

Bismuth.—Bismuth subsalicylate has been used for years almost as a routine throughout the course of malaria. A review of many of these charts shows no constant change in the course of the malaria which could be attributed to this drug. It may be that some of the "spontaneous terminations" seen occasionally were the result of this cumulative bismuth action, but unexplained termination of malaria is also seen when no bismuth is employed.

Both the oral and intramuscular preparations of sobisminol have been used. One patient, chilling every forty-eight hours (average temperature elevation of 40 C.), who had had nine paroxysms, was given three capsules (0.75 Gm., each 0.15 Gm. of metallic bismuth) three times daily for seven days. After the second day the temperature rose to 39 C. (102.2 F.) and fluctuated between 38 and 39 C. (100.4 and 102.2 F.) for the next seven days, then dropping to normal for seven days before quinine was instituted. Parasites were found during the first seven day period but none were found later. A 2 cc. intramuscular injection of sobisminol (0.04 Gm. of metallic bismuth) was given during each of the fifth, sixth and seventh chills. They were reduced in severity, but subsequent temperature rises regained the original level.

Biliposol (2 cc. contains 0.08 Gm. of bismuth), a liposoluble compound which should give a very high bismuth level in the blood stream, was used in three cases. In the first case three daily injections were given. The patient had one chill after the last injection (his sixth chill) and there were no subsequent chills for a period of thirty-two days, during which time the patient was receiving typhoid vaccine. No parasites were found on repeated blood smears. In the second instance four daily injections of the drug were given after the patient had completed his fourth daily chill. The fifth chill was unaltered but the sixth and seventh were reduced in intensity, and no additional paroxysms were observed in the following fifteen days during which time typhoid vaccine was used. However, it was possible to demonstrate an occasional malarial organism in the peripheral blood during the observation period. Results were not satisfactory for the end desired.

Sodium bismuth tartrate was given to four patients in injections of 4 cc., since 2 cc. apparently had no effect. Two patients received two daily treatments, one

¹⁹. Ampules of sodium thioglycollate were furnished by Parke, Davis & Co. for this study.

received three and the last received four. In no instance was any appreciable change produced.

Bithoxyl (an experimental liposoluble compound in which each cubic centimeter contains 0.06 Gm. of bismuth) was used for seven observations. Two patients received two 2 cc. injections, two received three, two more five, and another six. The first four patients (those receiving two and three injections respectively) showed no change in the course of the malaria. In the last three (receiving five and six daily injections respectively) the malaria was interrupted for the periods of observation, four, seven and twelve days respectively.

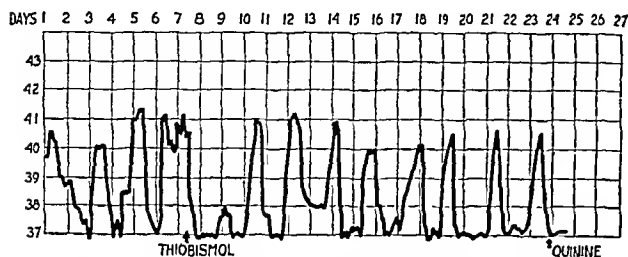


Chart 1.—Rest period provided in tertian cycle by single injection of thio-bismol 0.2 Gm.: Number of observations, seven cases. Rest period with reversion to tertian cycle, five cases; Failures: permanent cessation, one case; no effect, one case. Percentage of satisfactory results, 71.43.

No parasites were found in any case. Results were inconclusive for the effect desired.

Iodobismitol was used in eight instances. Two of the patients were given the drug before and during the incubation period after malarial inoculation; these patients did not take. In the remaining six the medication was used after the cycle had been established and from nine to eleven days after the bismuth had been started (the patients having had from three to six chills) the paroxysms ceased for observation periods varying from five to twenty-one days.

Thio-bismol was used in 103 observations, ninety-two of them with a single injection and eleven with more than one injection. The dose employed was the routine intramuscular 0.20 Gm. In general there were three types of malarial cycles in which it was used. The early prolonged prodromal remittent rise was encountered in from one third to one half of the patients inoculated intravenously; there was a second group in which a double cycle was encountered; finally there was a smaller group in which the fever originally assumed a tertian cycle. By far the greatest usefulness of thio-bismol is found in its effect on the prolonged remittent temperature rise and in the double tertian type of cycle. Moreover, it is in these groups of patients that untoward effects from the fever therapy are most common.

POSSIBLE RELATION OF ABSORPTION AND EXCRETION OF THIO-BISMOL TO THE PROBLEM

Thio-bismol is rapidly assimilated and excreted. Sollmann, Cole and their co-workers have shown that an injection of the drug is virtually absorbed and excreted within twenty-four hours. Thio-bismol is sodium bismuth thioglycollate $\text{Bi}(\text{SCH}_2\text{CO}_2\text{Na})_3$ and contains approximately 38 per cent of bismuth. The average 0.20 Gm. intramuscular dose contains 75 mg. of metallic bismuth. It has been shown²⁰ that the bismuth level in

the blood stream as measured by urinary excretion reaches a very high level within a matter of hours and then even as rapidly drops. Perhaps this may explain why some bismuth preparations have little or no effect on *Plasmodium vivax*. They do not reach this high level, transitory it is true, in such a short time.

RESULTS FROM INJECTION OF THIO-BISMOL

The value of the thio-bismol injection is in temporarily arresting the course of the therapeutic malaria. A single injection of this drug given just before a chill will bring about nearly always within six to twelve hours a rest period from the fever. The change produced in the type of chill which is to follow depends on the type of cycle which was present when the medication was given.

Prolonged Remittent Fever.—A forty-eight hour respite is the rule if the patient is suffering from a prolonged, tiring, constant, febrile attack. If untreated, this type may occasionally persist for eight or even ten days, if the patient does not succumb before that. During this respite the patient is afebrile, has none of the symptoms associated with the febrile phase of the disease and is able to take nourishment and important fluids that he could not formerly retain. After a two day rest the paroxysms return on alternate days (chart 1).

Daily Cycle.—If, on the other hand, the patient is chilling daily (double tertian) a single injection of thio-bismol will again remove one of the cycles so that a forty-eight hour rest period is provided and the patient continues to chill, not every twenty-four hours but every forty-eight hours (chart 2).

Alternate Cycle (Tertian).—When an injection of thio-bismol is given to a patient chilling every forty-eight hours, the results are not so predictable. Usually (if it is given early in the course of the malaria) only one chill is eliminated, giving an additional forty-eight hours rest. Then the cycle continues. If the drug is given more than ten hours before the next expected chill (by which time the drug will have been excreted) no effect is observed (chart 3). Rarely a single injection will terminate the clinical malaria entirely, though para-

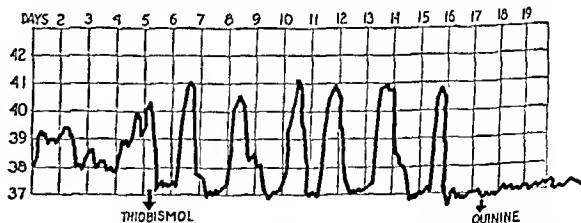


Chart 2.—Interruption of prolonged remittent fever by single injection of thio-bismol 0.2 Gm.: Number of observations, forty cases. Reversion to tertian cycle, thirty-seven cases. Failures: permanent cessation, one case; no effect, two cases. Percentage of satisfactory results, 92.50.

sites may be found in the blood after stimulation with epinephrine. The apparently inconsistent reactions to thio-bismol in this group are readily understandable when one remembers the rapidity with which the drug is excreted. The bismuth is almost entirely eliminated within twenty-four hours and the blood therapeutic level has been exhausted hours before that. Hence there may be no appreciable number of parasites in the blood stream at the time the bismuth is at a therapeutic level. This is not true in the first two groups of patients, for here the chills are persistent or occur every twenty-four hours.

20. Sollmann, Torald; Cole, H. N.; Henderson, Katharine; Binkley, George W.; Connor, W. H., and Sullivan, Maurice: Clinical Excretion of Bismuth: II. The Urinary Excretion of Bismuth After Clinical Intramuscular Injections of Sodium Iodobismuthite (Sodium Bismuth Iodide, Iodobismitol) and Sodium Bismuth Thioglycollate (Thio-Bismol), *Am. J. Syph., Gonorr. & Ven. Dis.* 21: 480 (Sept.) 1937.

VALUE OF THE THIO-BISMOL CONTROL OF
THERAPEUTIC MALARIA

Before we were acquainted with the action of thio-bismol, patients in an unfavorable condition were deprived of an opportunity to continue malaria therapy, as quinine usually terminated the course. It was very difficult to work out a dose that would temporarily stop the chills. Or if the patients were allowed to continue having paroxysms in spite of unfavorable clinical or

Effect of Single Injection of Thio-Bismol on Therapeutic Malaria

A. Effect on prolonged remittent fever:	40 cases
1. Rest period of 48 hours with reversion to tertian cycle...	31
2. Temporary interruption for 3 to 5 days with reversion to tertian cycle	6
3. Permanent cessation	1
4. No effect	2
B. Effect on double tertian cycle:	45 cases
1. Rest period of 48 hours with reversion to tertian cycle...	38
2. Temporary interruption of 3 to 5 days with reversion to tertian cycle	6
3. Permanent cessation	1
C. Effect on tertian cycle:	7 cases
1. Temporary interruption of 3 to 5 days with reversion to tertian cycle	5
2. Permanent cessation	1
3. No effect	1

laboratory evidence, serious, even fatal, complications were too common results. Through the use of thio-bismol the cycle can be altered, giving the patient a one or two day rest period in which to recuperate. Usually this interval is sufficient so that the patient may then be allowed to resume a further cycle and continue until there has been a sufficient number of therapeutic chills. If, however, the respite has not been enough to bring this about and the condition of the patient is still precarious, quinine can then be given to terminate the malaria completely.

Usually the rest period is sufficient to allow recovery from (1) prolonged exhausting fever, (2) weakness and prostration, (3) impending vascular collapse, (4) protracted vomiting, (5) rapidly developing anemia, (6) increasing icterus, (7) rapidly rising blood urea nitrogen.

The table shows that in forty cases of prolonged remittent fever after a single injection of the thio-bismol a rest period of plus or minus forty-eight hours resulted in thirty-one cases, and there was a temporary interruption for from three to five days in a further six cases. In forty-five cases of double tertian malaria a single injection caused a rest period for plus or minus forty-eight hours with reversion to the tertian cycle in thirty-eight cases and a temporary interruption of from three to five days in a further six cases. In seven cases on the tertian cycle there was a temporary interruption of from three to five days in five cases. In the entire ninety-two cases there were but four cases with no effect after the single injection of thio-bismol.

CASE STUDIES

Presentation of three typical cases will demonstrate the results of therapeutic malarial control by thio-bismol:

CASE 1.—E. B., a woman aged 30, with a diagnosis of paresis sine paresi, had an initial prolonged remittent type with daily temperature elevation varying from 40.5 C. to 41.6 C. (from 104.9 to 106.4 F.) and not dropping to normal for a period of six days. At this time she showed evidence of

prostration. She took little food or water and vomited what little she had taken. The blood urea nitrogen (which had been normal at the onset) rose rapidly to 40 mg. per hundred cubic centimeters. An injection of thio-bismol (0.2 Gm.) was given. Within eight hours the temperature had dropped to normal and remained so for the next forty-eight hours. This respite was sufficient to allow the patient to gain the rest and nourishment she needed. Blood urea nitrogen fell to 21 mg. per hundred cubic centimeters and the patient was deemed strong enough to continue. As expected, the chills resumed spontaneously after forty-eight hours and chills of a good intensity, from 40 to 41.4 C. (104 to 106.5 F.) proceeded at regular forty-eight hour intervals. The patient was allowed to have six additional chills (total twelve) without further difficulty. The blood urea nitrogen was down to 12 mg. per hundred cubic centimeters after the twelfth paroxysm.

CASE 2.—A. V., aged 64, with a diagnosis of early dementia paralytica, had been chilling on alternate days for three paroxysms. The fourth elevation remained at a persistent level of 41 C. (105.8 F.) for two days; during this time there was evidence of exhaustion; the blood urea nitrogen was 16.6 mg. per hundred cubic centimeters and the icteric index was 14 units. The usual dose of thio-bismol was given. The temperature returned to normal in seven hours and remained so for the next forty-eight hours. There was immediate improvement and the patient tolerated eight more much needed malarial bouts, which came spontaneously every forty-eight hours. At the end of the desired course of hyperpyrexia the blood urea nitrogen was normal, 11.2 mg. per hundred cubic centimeters, and the icteric index was 7 units.

CASE 3.—J. A., a man aged 48, with a diagnosis of dementia paralytica, was having severe daily chills, the temperature reaching 41 C. (105.8 F.) and maintaining the level for from eight to ten hours. During the fifth such cycle the patient showed signs of physical exhaustion and of vascular collapse. He was unable to take anything by mouth. There was a profound delirium and a falling blood pressure, 84 systolic, 40 diastolic. Thio-bismol was injected intramuscularly and the temperature fell to normal in six hours. The blood pressure responded, returning to 110 systolic and 60 diastolic, the sensorium became clear, and in general his condition was again quite good. After forty-eight hours the sixth chill came on spontaneously and he continued to have alternate paroxysms until he had received a total of eleven good reactions, at which time quinine was started. The blood chemistry showed but little change throughout the entire course of treatment.

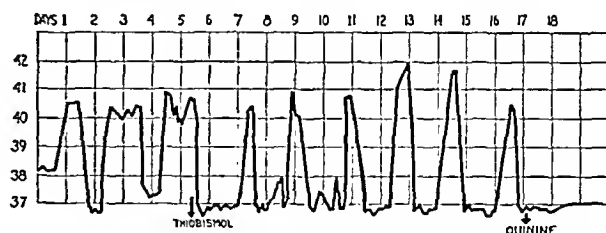


Chart 3.—Double tertian infection changed to tertian by single injection of thio-bismol: Number of observations, forty-five cases. Reversion to tertian cycle, forty-four cases. Failure: permanent cessation, one case. Percentage of satisfactory results, 97.77.

OTHER EFFECTS OF THIO-BISMOL

The main purpose of this study was to learn a method of managing therapeutic malaria without stopping the fever altogether, so that the value of the therapeutics would not be lost. However, it is worth mentioning briefly other actions of thio-bismol in malaria. Many times a patient will have one or even two additional chills after quinine therapy has been instituted to end a course of malaria. Most of the time this is not undesirable, but occasionally this added chill may be more than the patient can tolerate. To prevent this thio-bismol is given and quinine started at the same time.

The thio-bismol will eliminate the next expected chill, and by that time the quinine has become effective. This procedure is especially valuable if the patient is vomiting. Another method of preventing "added" chills, when it is desirable to stop the malaria, is the use of repeated daily injections of thio-bismol. With three daily injections it was found that paroxysms were terminated for periods varying from five to thirty-nine days before quinine was given. Further, in the unusual instance when the disease is resistant to ordinary antimalarial drugs (quinine or atabrine) the use of thio-bismol along with these drugs seemed to enhance their antimalarial properties, as was found in two quinine resistant malarias of the asexual strain.

RESULTS OF THIO-BISMOL TREATMENT

In the period of time since we have been employing thio-bismol to alleviate the effects of therapeutic malaria, 263 patients have been treated in our wards. It is true that our cases are in part selected in type. It is not possible to handle advanced mental cases in the service. Some of our patients, however, are quite degenerated and by no means good risks. During this period our mortality rate has been 2.24 per cent. There were six deaths, one from heat exhaustion, three from cerebral thrombosis, one from pyelonephrosis in a patient with a horseshoe kidney, and one from spontaneous rupture of the spleen. Moreover, as a result of the beneficial effects of the thio-bismol our patients almost without exception have been able to take a full complement of fever treatments, something that would have been impossible in the past.

The following two cases illustrate what may occur in any ward where this drug is not employed to take full advantage of malarial therapy. Both patients were treated with the same strain of benign tertian parasite that is being used today. These two patients were treated just before Schwartz had found the value of thio-bismol, and it is interesting to conjecture as to the ultimate outcome had thio-bismol been employed:

CASE 4.—A. B., a man aged 44, with a diagnosis of dementia paralytica, was chilling daily. By the time he had had seven paroxysms, the blood urea nitrogen had risen to 42 mg per hundred cubic centimeters. Intravenous dextrose, parenteral fluids and 5 cc. of 10 per cent quinine dihydrochloride intravenously were given. In spite of this his condition grew steadily worse and he died. The problem in this instance seems to differ very little from case 3, in which thio-bismol was given and the patient survived.

CASE 5.—F. G., a man aged 40, with a diagnosis of dementia paralytica, had a long, persistent prodromal elevation, which lasted for five and one-half days (from 39.8 to 40 C., or 103.6 to 104 F.). At the end of this time his condition was not grave, but progress notes indicated that fluids and food were refused and the patient was "very restless." After four additional chills the patient showed signs of impending vascular collapse, and supportive measures were given. Quinine urea hydrochloride 0.5 Gm. was given intramuscularly and quinine sulfate 10 grains (0.65 Gm.) was given by mouth. The patient did not respond to this, the temperature failed to drop, and he died. Case 1 of our series was much like this case and responded to thio-bismol.

COMMENT

The question naturally arises whether this peculiar action of thio-bismol is truly antimalarial. Such apparently is the case. Further, it is difficult to explain the selective action on alternate cycles of malaria unless on the basis that the drug acts most on that set of parasites which are at a certain stage of maturation.

It seems fair to conclude that the bismuth itself is the responsible component for the antimalarial action of thio-bismol. The vehicle of the preparation (sodium thioglycollate) was given in doses as large and even exceeding the amount given in the usual dose of thio-bismol, and it produced no effect whatever on the malaria. In fact, this study has been confined mostly to thio-bismol, and it is quite possible that further investigation will reveal other bismuth preparations that will have even as great an effect in therapeutic (asexual) malaria. After all, some of our observations with other compounds were not in sufficient number to be statistically of value. Shortly after an injection of thio-bismol there is a rapid but transitory high level of bismuth in the blood stream. It is quite possible that this high level as measured in terms of urinary excretion may explain the value of the drug in this particular situation.

SUMMARY

1. Therapeutic malaria employed in the treatment of central nervous system syphilis sometimes leads to one or more of the following alarming symptoms: (a) prolonged remittent fever, (b) physical exhaustion, (c) vascular collapse, (d) persistent vomiting, (e) an increasing anemia, (f) rapidly rising icteric index, (g) rapidly rising blood urea nitrogen.

2. If an agent could be found that would temporarily stop the course of the malarial chills, with rest thus furnished, it might be possible then to continue the chills to a satisfactory completion of the course.

3. Studies made with various selected heavy metals indicate that, while antimony compounds may in part satisfy this demand, certain bismuth salts, and more particularly thio-bismol, answer the requirements.

4. In the one to three day rest period from the chills, the fever drops, exhaustion, vascular collapse and persistent vomiting disappear, the blood urea nitrogen and the icteric index fall, the blood pressure rises to more normal levels, and with resumption of the chills the patient's increased strength allows him to go on to a completion of his course of chills.

5. The action of the thio-bismol and of other bismuth salts seems to be a bismuth effect on the malarial parasite. Its success may depend on the rapid attainment following the bismuth injection of a high transitory bismuth level in the blood stream as measured in terms of bismuth excretion in the urine.

6. Repeated injections of bismuth, especially thio-bismol, stopped therapeutic malaria for long observation periods (as long as thirty-nine days).

7. It is not to be assumed that we offer thio-bismol as a substitute for quinine in terminating malaria, but we do maintain that thio-bismol is a reliable drug in the management of therapeutic malaria and by its use many untoward therapeutic malarial results can be avoided.

8. Moreover, where it is desired to terminate a course of therapeutic malaria without shock to the patient, it will be found that an intramuscular injection of thio-bismol plus quinine or atabrine by mouth will accomplish this.

9. With the use of thio-bismol as indicated in 263 cases of therapeutic malaria in our wards, the death rate was 2.24 per cent. Moreover, with the help of the drug it was possible to carry on the course of malaria until the patients had had an adequate number of hours of hyperpyrexia.

ABSTRACT OF DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: A survey of the value of mechanotherapy and malaria therapy by a group interested in both types of fever therapy was recently completed. The parallelism in both the therapeutic results and the serologic results was striking in a group of patients with dementia paralytica treated and observed for more than five years. Therapy by mechanical means has a few advantages and malarial therapy likewise has a few advantages, but it was obvious that the outstanding disadvantages of malaria were the points that the authors have called attention to, namely exhaustion, debility and anemia. It has been the inability heretofore to control the intensity of the malarial reactions satisfactorily that has justified some criticism of this type of fever therapy. Thiobismol as a modulator of malaria therapy has greatly reduced the intensity and severity of these reactions. Dr. Cole suggested the value of thiobismol as a modulator to me and during the past few months I have given it to thirty out of ninety patients undergoing malaria therapy. The "comeback" following an injection of thiobismol of the individual who has become exhausted and debilitated from the malaria course is striking. It has been my experience that in the small individual who weighs less than 115 or 120 pounds (about 53 Kg.) it is advisable to use less than 1 cc. of the thiobismol. I observed one patient who went for eight days without chills or fever following the thiobismol and whom it was necessary to reinoculate with *Plasmodium vivax*; in other words, to reinduce the malaria. I do not mean to imply that thiobismol is curative as regards malaria, but the drug ameliorated the infection to the point that it was necessary to reinoculate her and start the fever course again. I do not know what influence thiobismol will have on the clinical and serologic results from malaria therapy. I cannot imagine that it will influence the results of this type of fever therapy in any way whatever. When thiobismol is given to a patient who is having a severe course of chills and fever from malaria, we do not decrease the total hours of fever in that patient but merely extend the number of hours of fever over a longer period. The value of fever per se versus some biologic factors in producing the good results of this type of therapy has not been determined. Thiobismol does not influence the temperature curve as far as the height of the fever is concerned, but it does permit of giving more fever bouts than has been the custom in the past. This is permissible because it is now possible to control the cachexia, debility and so on. This suggestion of Dr. Cole and his co-workers is valuable to those still interested in malaria.

DR. HAROLD N. COLE, Cleveland: I wish to give Dr. Schwartz of Pasadena, Calif., full credit for discovering this little trick, if you may call it that. In our work with bismuth excretion, occasionally we had to fall back on a patient with malaria as the guinea pig, as there was nobody else available in the ward. Schwartz noticed in some of these patients that following the injection there was a peculiar disturbance of the chills and he was unable to correlate it. After following a few of these he called this to my attention. It seems to be the bismuth radical that causes this for we have made experiments with the thioglycolate and find that it has no effect on it. Apparently there are other heavy metals that have an effect on malaria. The difference, however, is that you can't predict what they will do. They may stop it or it may require several injections. We have found that it has been a valuable addition to our armamentarium and that now practically all of our patients are able to have their full complement of chills where, in the past, many times it was necessary to give them quinine to save their lives.

Temper Tantrum.—If dealing with a long-continued and strongly developed behavior pattern, complete reliance upon a discourse seems to me like using a garden sprinkler to extinguish a two-alarm fire. Talking a child out of a violent temper tantrum, for example, is about as sensible as trying to allay hunger with an oration. Immobilization in blankets will calm him; spanking will only increase the excitement of an angry child.—Holman, Leslie B., *As the Twig is Bent*, New York, Macmillan Company, 1940.

PROGRAM FOR INDUSTRIAL HEALTH
IN STATE AND COUNTY
MEDICAL SOCIETIES

CHARLES-FRANCIS LONG, M.D.

Chairman, Committee on Industrial Health, Medical Society
of the State of Pennsylvania
PHILADELPHIA

Sometimes it is a pleasure not to have to begin at the beginning. In a speed-up era such as this is, I find it gratifying to be able to streamline the work of the Council on Industrial Health of the American Medical Association into one phrase, justly stating that its foundation work is so fine and familiar to all of us that we can move immediately to our problem at hand; that is, the setting up of committees on industrial health in the state societies and in the county societies.

Predicated on the good will of society presidents and boards of directors, these state committees spring easily and simply into being. And yet we know that only two thirds of our state societies have committees on industrial health, perhaps because there are still those in office among us who carry over into the present the old umbrage against the so-called "contract physician" and act as obstructionists accordingly. They do not yet appreciate that industrial health is the deep concern of every American physician and that our parent organization has gone far in comprehending this vision.

First of all, the state committee should represent all districts of the state, the general practitioner and the medical teaching faculties wherever they are present. Even more important, it should represent the medical services of large and small industries. It is a moot point whether the state department of health should be represented on the membership or whether this body should be contacted in a consulting capacity whenever needed. We feel definitely though that here is not the place for members from the specialist consulting group, for they are on the second line to be called by those who are already represented.

On its establishment, it is probable that the committee will immediately be faced with external and internal problems. The field of industrial medicine has not even been surveyed. It has lain fallow for so long that much needs be done before it can even be worked, much less be made to produce. This leads us to a plea for our newly appointed state committees on industrial health—no members who are subject to yearly appointment by changing presidential candidates can ably adopt and carry through a long-time, well planned program such as is required. It is highly important then that the committee be changed to a commission or some such more permanent form of setup, perhaps with staggered appointments so that there may be complete continuity of thought and effort.

Once the state committee form has been determined, its first efforts should be the establishment of county committees on industrial health in 100 per cent of the counties of the state. Naturally, the experience will vary from state to state in direct proportion to the number of industrial and rural counties contained within its borders. The simplest method is a letter from the chairman of the state committee to the president of

the county society strongly urging the appointment of such a group and, if desired, giving suggestions as to ideals, aims and personnel. Gaged by the Pennsylvania experience, the industrial counties will respond promptly.

The establishment of these county committees seems doubly important. The individual physician and the individual industrial plant can be best reached by county contacts, and both need a reference group to guide and review policy. The state committee too needs the county committee as its liaison with the individual practitioner, and the county committee needs its state

TABLE 1.—Plant Size in Pittsburgh Area

Manufacturing establishments.....	1,906	Employees	189,807
Mines	50	Employees	14,682
Total	1,956		204,489
Employing 250 or more.....	127		6%
Employing less than 250.....	1,829		94%

committee as liaison with the American Medical Association. Thus we have both a descending and ascending essential chain of communications.

In Pennsylvania we have set ourselves a goal which gives opportunity for a tremendous amount of work. We aim to "assure the best possible health to every worker in every industry within the state." This must be gradually approached by a coordinated program between the state and county committees and industrial organizations and labor groups. The first efforts must be a survey of the field, as we realized at our initial meeting. We proposed to do this by a questionnaire to all the physicians of the state, by data from the Department of Industrial Hygiene, and data from the chambers of commerce. Our results have been highly discouraging to date. The chambers of commerce have no data of any use to us. The Department of Industrial Hygiene has important data but it is not in a form that can be obtained without putting extra hands to work, and at present there is no money to pay the extra hands. We had hoped that at least the physicians of the state would not fail us, but they almost unanimously did. We have roughly 9,000 members in our state society. In two consecutive issues of the state medical journal we printed identical questionnaires to be returned to our committee. Of those 9,000 members, only 220 responded. But not all was completely lost. Through the question "Are you an industrial physician?" we discovered many more physicians doing industrial medicine and interested to learn more about it than any of us had suspected. This, I should say, was the only benefit we derived from the questionnaire.

However, the conviction still remains that no problem can be solved without knowing its extent. The questions which must be answered by the state committee are:

1. How many physicians are already rendering medical service to industry?
2. How many practicing physicians will devote time to learning the fundamentals of industrial health in a refresher course?
3. How many industries in the state employ 1,000 or more workers and do they have plant physicians?
4. How many industries in the state employ 250 or less workers?

Our experience would warn that the questionnaire method as we have used it is uninformative. However,

this does not exhaust the possibilities or scuttle the questionnaire method. It merely proves again that personal appeal is better than eye appeal. Two suggestions for improved returns can be offered:

1. At the annual convention of the state medical society, persuade the members to answer the questionnaire as a part of their registration procedure. This has one drawback in that only 20 to 25 per cent of the total membership will attend the convention. Even at that, the figures would be better than our method has given us.

2. Send sufficient copies of the questionnaire to the secretary of each county medical society with the request that they be filled out at the next regular meeting of the society, collected at the end of the meeting and mailed back to the state committee. This, I believe, will be likely to yield the best results.

For figures on the industrial setup in each state, if your state is like mine, the state department of labor will have a census of industries showing distribution by counties and number of employed personnel, so that at least some idea can be gained as to the size of the potential demand for industrial health service. It can be taken as a good rule of thumb that industries employing 250 or less individuals have now no medical service, with the exception of those rare few who recognize that they have a peculiar industrial or toxic hazard.

The next step might be termed the sowing of the field and, as Dr. Howard Haggard put it so well recently in Philadelphia, "We must change a lot of people's folk-ways." The state committee must busy itself in assisting the practicing profession to develop adequate programs of industrial hygiene successfully in industries great and small. Let us honestly admit, right now the profession is not trained to take over such a job. We are not prepared to meet the employer's requirements or to meet the employee's expectations. The state committee should therefore be ready to submit a curriculum for refresher courses on industrial health, workmen's compensation laws and occupational disease laws to the county societies or to any other interested medical group. Whether there should be peripatetic teaching units sent throughout the state will depend on the judgment of each committee.

TABLE 2.—Plant Size in Philadelphia Area

Manufacturing establishments.....	5,537	Employees	292,691
Employing 250 or more.....	232		4%
Employing less than 250.....	5,305		96%

Further, there is a lamentable lack of familiarity with industrial health among the vast majority of our medical students. Less than 10 per cent of our seventy-seven medical schools give required undergraduate instruction in this subject, and only a few of these courses could be considered "adequate." Naturally the argument is advanced that medical school curriculums are already overcrowded and why crowd more in? We need only shift our faculty field of vision a little more toward preventive medicine than it now sees, and the curriculum time will be found. It has been allotted in the more forward looking schools, and with the help of state committees it will be provided in the rest.

Education of the employing and employed public need not require too much of our endeavors. That education is coming along rapidly enough. The various commit-

tees on industrial health of chambers of commerce and Dr. Victor Heiser's committee of the National Association of Manufacturers are seeing to it that industrial health publicity reaches into many trade journals throughout the country. You all doubtless realize that industrial health must be "hot news" if the *Saturday Evening Post* published such an excellent article as that recently written by Dr. Schramm.

The state committee will find that its work inevitably will cross many borders. It must be interested in medical ethics, in existing and new medical and workmen's compensation laws and in the fight against socialized medicine. This entails a complete rapport between itself and the other committees of the state society. But, consisting as it does of men from every corner of the whole state, it is physically impossible for the committee to have frequent joint meetings with these groups. So, unless some simpler method is devised, many joint problems remain unsolved. It is my suggestion that contact with individual committees be maintained by a single member of the committee on industrial health for each particular activity, relying on his good judgment to act for the whole committee.

As is generally true in the American scene, a fine program can succeed or fail depending entirely on local applications. Herein lies the exceeding importance of the county committees. It falls to their lot to apply the principles established by the state committee with due regard for local variation. It is up to them to smooth the relationship between industrial physicians and general practitioners. They must show the industrial physician that his field is entirely intramural, that it must be kept within the confines of the working place, stepping out only when the workmen's compensation or occupational disease laws require him to do so. These committees must show the general practitioner that the industrial physician is a case finder for him and should be treated with at least as much good grace as an old patient who brings a new one to the office.

Finally, these committees have probably the biggest job of all. It is for them to consult with employer and labor groups in providing adequate medical services to all types of workers. Paradoxically, the difficulty and need for this phase of county committee work increases as the size of the plant decreases. Let us again turn to our experience in Pennsylvania and to our two largest industrial counties, Philadelphia and Alleghany.

Philadelphia County contains 5,537 manufacturing establishments employing 292,691 individuals. But only 232, or 4 per cent, employ 250 or more employees, so that 96 per cent of all manufacturing in this county is done in plants employing from one to 250 workers. In Alleghany County the story is similar. There are 1,956 industrial firms and mines employing 204,489 persons. One hundred and twenty-seven, or 6 per cent, have 250 or more employees, or, putting the converse again, 94 per cent of all manufacturing here is done in very small plants. From these figures it is evident that 95 per cent of all industrial establishments in these counties employ less than 250 workers. Here then lie our greatest opportunities for improving industrial health. Such opportunity must be within the province of the county committees on industrial health. Their question at the moment is how to provide medical service to these small plants on an ethical basis and at a bearable cost. The answer will be furnished by demonstrations which can be successfully staged only with the active help of the county committee.

Such demonstrations have been attempted under lay auspices but not with marked success. With the help of the county society, through its committee on industrial health, demonstrations should be arranged that can forcefully and honestly depict medical service to small plants. Only by such demonstrations can the county society keep abreast of the times and assume its rightful leadership as professional director of lay interest in medical activities.

1836 Delancey Street.

HISTAMINASE IN THE TREATMENT OF ALLERGIC DERMATOSES

LAWRENCE C. GOLDBERG, M.D.

CINCINNATI

The discovery by Best and McHenry¹ of an enzyme which specifically inactivates histamine suggests its use in the treatment of allergic cutaneous disorders. It has been shown that there is a release of so-called H substance in the blood during allergic shock and that this H substance may be histamine. Innumerable writers have endeavored to demonstrate the fact that histamine must be the trigger mechanism which prepares the skin for various reactions, particularly the so-called triple response of vasodilatation (streak), wheal exudative (edema) and reflex nervous dilatation (flare), which is dermatographism or urticaria itself.² If this fact is true, then the assumption that treatment of these allergic states with histaminase is well founded and worthy of an extended trial before being discarded as another false hope in the long list of attempts to combat the allergic dermatoses.

Histamine may be obtained from the liver, lungs, skin and other body tissues in a pure form under aseptic conditions.³ It is preformed in the cell in a slightly inactive form and is readily released into the surrounding area. This release is not entirely dependent on the destruction of the cells but may occur when the cells receive stimulation of a certain intensity, and the magnitude of this stimulation is dependent on the allergic irritability of the individual cells. The fact that very little histamine is found in the urine after the intravenous injection of large amounts of the substance⁴ led Best and McHenry to study distribution, properties and action of the substance or system producing this inactivation.

Histamine inactivating material was first demonstrated in horse lung and subsequently in beef lung, liver and kidney. The kidneys, duodenum, jejunum and cecum each inactivated the greatest amount of histamine, and the kidney was more active than any other tissue in inactivating histamine.

Histaminase is a compound of physiologic albuminoid substance obtained from the intestinal mucous membrane. It is a loose white powder which is stable and

Read before the Section on Dermatology and Syphilology at the Ninety-first Annual Session of the American Medical Association, New York, June 12, 1940.

The histaminase was supplied by M. A. Hilger of the department of medical research of the Winthrop Chemical Company, Inc., which markets this product under the proprietary name Torantil (T 360).

1. Best, C. H., and McHenry, E. W.: The Inactivation of Histamine, *J. Physiol.* 70: 349 (Dec.) 1930.

2. Stokes, J. H.; Kulchar, G. V., and Pillsbury, D. M.: Effect on the Skin of Emotional and Nervous States, *Arch. Dermat. & Syph.* 31: 470 (April) 1935.

3. Best, C. H.; Dale, H. H.; Dudley, H. W., and Thorpe, W. V.: The Nature of the Vasodilator Constituents of Certain Tissue Extracts, *J. Physiol.* 62: 397 (March) 1927.

4. Ochme, C.: *Arch. f. exper. Path. u. Pharmacol.* 72: 76, 1913.

dissolves in water to a slightly opalescent fluid. This preparation is put up as a dry powder of 2 histamine detoxicating units and in tablets enterically coated of 5 units. The unit is the amount necessary to inactivate 1 mg. of histamine during twenty-four hours' incubation at 37 C. in a phosphate buffer solution at a p_H of 7. Chemically histaminase is diamineoxydase.⁵ The change produced in histamine during inactivation appears to be oxidative since it is inhibited by potassium cyanide, and under anaerobic conditions it is accelerated by oxygen. It is suggested that rupture of the iminazole nucleus occurs in the histamine or that a complex nondialyzable compound is produced. Reduction of the iminazole value parallels the degree of inactivation of histamine.

Roth and Horton⁶ determined the normal response of gastric acidity to subcutaneous injection of histamine. Several days after the response had been accurately established, histaminase was introduced into the duodenum from twenty-five to thirty minutes before the subcutaneous injection of histamine. This practically abolished the rise of gastric acidity. Likewise subjects were immersed in water at 24 C., and the curve of their gastric acidity under such conditions was similar to that caused by histamine. As before, the introduction of histaminase abolished the rise in gastric acidity. In similar fashion, when histaminase was injected intramuscularly thirty minutes before the usual subcutaneous injections of histamine, the rise in gastric acidity was abolished. This is physiologic evidence that histaminase administered to man will inhibit the action of histamine and contrary to the work of Atkinson and Ivy,⁷ although they injected their histaminase intravenously instead of introducing it directly into the duodenum.

Karady and Browne⁸ carried out experiments to determine what effect pretreatment with histaminase might have on histamine and anaphylactic shock in animals. They used thirty guinea pigs. The jugular vein of twenty pigs was exposed under slight ether narcosis and 3 units of histaminase dissolved in 2 cc. of physiologic solution of sodium chloride was injected. In fifteen minutes all thirty received 4 mg. of histamine dihydrochloride intra-abdominally. In from five to seven minutes all the nontreated animals were in histamine shock; seven died. Two of the pretreated animals died in thirty-five minutes; all the rest survived. Thirty guinea pigs were sensitized with 3 cc. of 50 per cent egg white subcutaneously. From two to three weeks later twenty guinea pigs were injected with histaminase under the same conditions as previously described. After fifteen minutes all received 2 cc. of 50 per cent egg white intra-abdominally. Four of ten animals of the control group died in from ten to fourteen minutes; all had symptoms of anaphylactic shock in four or five minutes. None of the pretreated group died.

Horton and Roth⁹ described a case of hypersensitivity to cold, which case they had followed since 1927. They concluded that urticaria produced by hyper-

sensitivity to cold was due to an overabundance of histamine. They treated their patient with subcutaneous injections of 0.1 mg. of histamine dihydrochloride weekly in an effort to increase the patient's tolerance to histamine. The patient improved. Later they¹⁰ treated a similar case with histaminase, administering 67 units in four and one-half days. He too improved.

Gilbert and Goldman¹¹ prepared bronchioles for microscopic examination. The size of the bronchiole was recorded by the use of a camera lucida. The addition of 3 mg. of histamine acid phosphate usually resulted in complete closure of the bronchiolar lumen. The preparation was observed for about ten minutes in order to rule out spontaneous relaxation and then the test drug was added. Histaminase caused slight dilatation of histamine-poisoned bronchioles in three experiments and no effect in two. After twenty-four hours' incubation at 37 C. a mixture of histaminase and histamine caused marked contraction of normal bronchioles in four experiments. Their conclusions were that histaminase is unable to prevent the action of histamine on these preparations.

Foshay and Hagebusch¹² believe that serum sickness with its urticarial manifestations is due to release of histamine in the tissues and circulation consequent on the union of serum protein antigens and antibodies. Six of eight patients with serum sickness received complete relief from 5 units of histaminase given orally three times daily. Within thirty-six hours all these patients had relief from their intolerable pruritus, patchy erythema and urticaria. Twelve patients were treated twice daily with the injectable form. Within seventy-two hours none of the patients had any further symptoms. They expressed optimism for the prophylactic use of histaminase in the prevention of serum sickness and further stated that this method of treatment is the only rational, genuinely effective and safe remedy known for this distressing condition. Moldenshardt¹³ treated five patients who had cutaneous disorders with histaminase, two of whom had eczema, one Quincke's edema, one a moist erythema associated with marked pruritus and one serum sickness following diphtheria antitoxin injections. All responded and recovered within a short time. Adelsberger¹⁴ reported excellent results with histaminase treatment in three cases of allergic eczema on a nutritional basis and one case of light dermatitis. Hartmann¹⁵ stated that twenty-five patients with severe acne conglobata who had failed to respond to all types of medical treatment showed remarkable improvement after four or five injections of histaminase. In most of the twenty-five cases there existed some digestive disorder. Blecha¹⁶ treated twelve children who had allergic eczema with oral and intramuscular histaminase; five were completely cured, three greatly improved and the remainder were unaffected. Laymon and Cumming¹⁷ treated seventeen

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8. Karady, S., and Browne, J. S. L.: Effect of Histaminase Treatment on Histamine and Anaphylactic Shock in Guinea Pigs, J. Immunol. 37: 463 (Nov.) 1939.

9. Horton, B. T., and Roth, Grace M.: Proc. Staff Meet., Mayo Clin. 12: 7 (Jan. 6) 1937.

10. Roth, Grace M., and Horton, B. T.: Proc. Staff Meet., Mayo Clin. 12: 129 (March 3) 1937.

11. Gilbert, A. J., and Goldman, F.: The Effect of Aminophyllin, Histaminase and Nicotinic Acid on Histamine-Poisoned Puppy Bronchioles, Bull. John Sealy Hospital and School of Medicine, University of Texas 2: 55 (March) 1940.

12. Foshay, Lee, and Hagebusch, O. E.: Histaminase in the Treatment of Serum Sickness, J. A. M. A. 112: 2398 (June 10) 1939.

13. Moldenshardt, H.: Torantil, ein aus Darmschleimhaut gewonnenes Präparat, Med. Klin. 32: 153 (Jan. 31) 1936.

14. Adelsberger, L.: Fortschr. d. Therap. 13: 568 (Oct.) 1937.

15. Hartmann, M.: Ueber die Behandlung der Akne vulgaris mit Torantil, Dermat. Wchnschr. 106: 693 (June 18) 1938.

16. Blecha: Med. Klin. 34, Feb. 11, 1938.

17. Laymon, C. W., and Cumming, H. A.: Histaminase in the Treatment of Urticaria and Atopic Dermatitis, J. Invest. Dermat. 2: 301-303 (Dec.) 1939.

patients who had urticaria with histaminase and recorded the following results: 59 per cent cured, 12 per cent improved and 29 per cent unimproved; no definite improvement in eight cases of atopic dermatitis, and it was of no value in two cases of dermatographism. Forman¹⁸ stated that this therapeutic agent offers a new and helpful approach to the treatment of urticaria, angioneurotic edema and atopic dermatitis. In his report of thirteen cases of urticaria, all but one showed improvement, two of three cases of atopic dermatitis showed improvement, two of four cases of contact dermatitis showed improvement and one case of pruritus was controlled by histaminase. Urbach¹⁹ reported the successful treatment with histaminase of a woman aged 31 with severe purpura; vitamin C had been tried without any beneficial results. He concluded that in this instance the purpura was due to a deficient detoxifying function of the intestine. Matras, in discussing this case, mentioned one of chronic urticaria which had not been benefited by injections of histaminase. Baker²⁰

Treatment with Histaminase

Diagnosis	No. of Cases	Results	Comment
Twenty-Five Cases Under Oral Treatment			
Papular urticaria	1	Clinically cured	Histaminase used alone
Atopic dermatitis	3	Improved	Histaminase in conjunction with other therapy
Dermatographism	2	Unimproved	Histaminase used alone
Allergic eczema	3	2 unimproved 1 improved	Histaminase in conjunction with other therapy
Chronic urticaria	13	8 clinically cured 5 unimproved	Histaminase used alone
Idiopathic pruritus	3	Slight improvement	Histaminase used alone
Ten Cases Under Injection Treatment			
Chronic urticaria	10	All improved	Fever up to 102 F. after first injection, general malaise, pain at site of injection; mild rises in temperature after second and third injections, very little thereafter

reported two cases of cold urticaria which responded to treatment with histaminase. The first patient had a severe generalized headache, palpitation and general tremulousness associated with the urticaria. These symptoms subsided with the onset of the localized edema. Histaminase tablets were used simultaneously with gradual desensitization to cold. The results of the treatment were most gratifying. The second patient was treated similarly with the same good results. Kile and Rusk²¹ treated a patient who had cold urticaria with histaminase without any results. They did not mention the amount used or the length of time it was tried. Miller and Piness²² treated forty-two patients with histaminase; twenty-nine had urticaria, and only five were relieved; five had allergic dermatitis, and none were relieved. They felt that in no instance could this

relief be unequivocally attributed to the use of the enzyme. They reported few untoward reactions.

The histamine-histaminase reaction is an oxidative one, and as yet I have observed no untoward reactions. There is no need to worry about the type of reactions that occur when a patient is treated with small doses of histamine such as flushing of the face, shivering or faintness, fall in blood pressure, rise in pulse rate, headache, anginal pains in the chest or shock.

My purpose in this paper is to picture the results of treatment of various allergic cutaneous disorders with histaminase, orally and by injection, and to demonstrate that it might be a valuable adjunct in the management of these cases. All the cases studied were taken from private practice and analyzed from the clinical point of view. In some of them histaminase was used by itself while in others it was a part of the advised therapy. When it was not the only therapeutic agent, the patients had been rebellious to other routine treatment measures. Twenty-five patients received histaminase by mouth; these may be subdivided as follows: thirteen had recurrent urticaria, three had allergic eczema, one had papular urticaria and three had pruritus. Ten patients with recurrent urticaria received intramuscular injections of histaminase 2 cc. every other day for a minimum of six injections and a maximum of twelve. The initial reactions of fever, malaise and joint pains following intramuscular injections of histaminase in 2 cc. doses suggests the possibility of a foreign protein reaction. However, the same type of reaction does not always occur after the second or third injection, which does not hold true for reactions following injections of whole milk and other nonspecific proteins. This requires further investigation of the injectable material. All the patients so treated showed marked improvement, and after treatment was discontinued no recurrences have been noted up to the present time.

SUMMARY

This group of thirty-five cases is too small a series to permit any dogmatic statements. In several cases the use of histaminase alleviated all the symptoms while in others it was a very useful factor in controlling the pruritus. Histaminase is no more a cure-all for allergic cutaneous conditions than are allergens the sole major excitants in the same diseases. Furthermore, it must be remembered that histaminase is a protein preparation and probably contains a variety of proteins which might cause reactions in patients whose allergy is of a protein type. It is possible that treatment with histaminase may give the epidermal structures relief from histamine excitation and help it build tolerance to histamine in the same way that intravenous injections with histamine in the treatment of chronic urticaria produces a gradual unresponsiveness of the skin to "H substance," which is thought to be responsible for whealing, as believed by Alexander.²³ I know that there has been no established fact that histamine is the causative agent in any pathologic condition and that most of the present data may be presumptive. Nevertheless evidence has been presented showing that histaminase oxidizes histamine in the body and on this basis its therapeutic assistance in the treatment of allergic dermatoses may be justifiable.

18. Forman, Jonathan: The Use of Histaminase in the Treatment of Various Allergic Manifestations, Ohio State M. J. 36: 56 (Jan.) 1940.

19. Urbach, E.: Intestinal-toxisch bedingter Charakter einer chronisch rezidivierenden Purpura durch Torantil festgestellt, Zentralbl. f. Haut. u. Geschlechtskr. 54: 70, 1936.

20. Baker, T. W.: Histaminase in the Treatment of Cold Allergy, J. A. M. A. 114: 1059 (March 23) 1940.

21. Kile, R. L., and Rusk, H. A.: A Case of Cold Urticaria with an Unusual Family History, J. A. M. A. 114: 1067 (March) 1940.

22. Miller, Hyman, and Piness, George: Histaminase in the Treatment of Allergy, J. A. M. A. 114: 1742 (May 4) 1940.

23. Alexander, H. L., and Elliot, R.: Treatment of Chronic Urticaria with Intravenous Injections of Histamine, read before the Central Society for Clinical Investigation in October 1939.

CONCLUSION

Histaminase oxidizes histamine in the body and is a helpful factor in the treatment of allergic dermatoses. A small group of thirty-five patients with various allergic dermatoses was treated with histaminase, orally and by injection. There was partial or total improvement noted in all but nine of the patients treated. I can draw no definite conclusions regarding the dosage of histaminase, since each case must be studied individually. However, as yet no untoward reactions have been noted after patients have taken as much as 150 histamine detoxicating units daily for four or five days. Patients receiving intramuscular injections of histaminase had very much better results than those receiving the enzyme in tablet form. The first four injections elicited symptoms comparable to those following foreign protein shock therapy. Further clinical and laboratory data are necessary before any definite conclusions can be drawn regarding the specific value of histaminase.

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ABSTRACT OF DISCUSSION

DR. G. MARSHALL CRAWFORD, Boston: Dr. Goldberg has reviewed the rationale of histaminase. Its physiology, chemistry and mode of action were discussed, but this is mostly presumed knowledge. It is also based on what is known or presumed about histamine and assumed that histamine is the so-called H substance. Failure of this presumably ideal treatment should lead us to doubt whether histamine is actually that H substance. At least it may not be the only H substance, or some other agent may play a part in certain cases. It seems to act as a trigger mechanism part of the time. If histaminase will break a link in the chain of the allergic reaction, that may be its most valuable function. This might increase the magnitude of stimulus necessary to initiate allergic reaction, in other words decrease the allergenic irritability of tissues. If so, this could allow us to work backward in determining the cause of allergy. Whether histaminase interrupts an antigen-antibody reaction or brings about oxidation or deamination could then perhaps be determined. Possible foreign protein action, as mentioned by Dr. Goldberg, should be considered carefully, especially with the intramuscular injection. A review of the literature shows that about a dozen conditions have been treated with histaminase. Best results were obtained in serum sickness, physical allergy, angioneurotic edema and some chronic urticaria. In other diseases, results are questionable. At the Massachusetts General Hospital we have studied about twenty-five cases, with the following results: Treatment of three actinic and one cold allergy cases gave fairly satisfactory results. The cold urticaria was completely relieved as long as the treatment was continued. Two cases of actinic urticarias were 80 per cent relieved and one *eczema solare* was untouched. Fifteen cases of chronic urticaria of from three months' to fifteen years' duration were unsatisfactory. In two the condition was somewhat worse, possibly because of pork sensitivity. Histaminase is obtained from the hog. We gave orally up to 300 units daily. Six cases of dermatographism were entirely unresponsive. Our resident, Dr. Capland, has followed these more closely and is more pessimistic than our results indicate. In physical allergy, however, there is a fair degree of success. Dr. Goldberg's emphasis on the presumption of the mode of action of this drug is well justified. I agree that histaminase is no cure-all, and I should like to reemphasize again the possibility of foreign protein action. The plea for further trial before discarding this agent is worth while.

DR. ASHTON L. WELSH, Cincinnati: I happen to have had the opportunity to use histaminase in a group of six cases of lichen urticatus. All six cleared completely on histaminase in large doses. Three were followed for more than one year and have remained clear. The other three were lost after from one to two months' observation. I have also had one patient with cold urticaria which has completely cleared and remained clear. Other patients with other forms of urticaria and with atopic

eczema did not show such a favorable response and have not been controlled well enough or followed long enough to admit of critical appraisal.

DR. HERMAN GOODMAN, New York: Success or failure of a drug such as histaminase depends on what one prescribes it for and when it is given. For many years it has been recognized that, no matter what the irritant, the effect on the skin has been very much the same. There are limited modes of reaction by the skin to numerous unrelated injuries or insults. In the discussion of histaminase in the treatment of allergic dermatoses, it is contended that the effect of histaminase is not on the irritant histamine in the sense that it has been mentioned this morning. The irritant effect is on preventing the formation of the histamine. Histidine is the precursor of histamine. Histamine is formed on injury to protein of which histidine is a component. Histidine is five times as prevalent in skin protein as any other tissue. To be effective, histaminase must prevent the decarboxilation of histidine. Therefore, to prevent the action of histidine it is necessary to have an agent, which histaminase is held to be, which will break the chain between histidine and histamine. The same agent fails if given long after histamine has done its damage. The greatest success of histaminase is in cold allergy, which is the response to insult to the continued presence of histamine resulting from decarboxilation of histidine. One does make it possible for the person to expose himself to cold without giving evidence of his cold allergy by reason of the fact that by the administration of histaminase the decarboxilation of histidine has been interrupted. Results are to be expected of histaminase if one recalls histidine, its decarboxilation, and the formation of histamine which is the activating cause of the response of the skin.

DR. HERMAN SHARLIT, New York: I want to endorse what Dr. Goodman just said. Histaminase cannot cure the condition which it alleviates. Histaminase succeeds, where it does succeed, only in placing a block in the machinery of the production of a sign, if given at a proper moment, and when removed has no influence on successive episodes in the production of the symptom. In other words, if we are dealing with a successful treatment of urticaria by histaminase, if on the cessation of the use of histaminase we get no further urticaria, the cure has not been achieved by the histaminase; whatever the cure, that remains a mystery; but histaminase has given the interim, has given the time to suppress symptoms to a time when they were no longer spontaneously produced. A patient had urticaria limited to the face for two years daily without interruption, in spite of every approach from the point of view of external irritants or ingested foods. Everything conceivable had been tried to stop this urticaria. When I first saw this victim, she was beginning to develop, in addition to hives, edemas of the lip and the eye. I gave her fifteen tablets of histaminase at once. The next day she had no urticaria for the first time in two years. She continued histaminase fifteen tablets a day for three days without any recurrence of the urticaria. On the fourth day I advised the reduction to two tablets three times a day and the urticaria returned. The situation is now exactly that, three months afterward: namely, so long as she takes fifteen tablets of histaminase a day, she has no urticaria; when she reduces it or gives it up for one day, the urticaria is back again. Until she either spontaneously breaks the causative link or it is discovered and destroyed, she will persist in having urticaria. But from the point of view of clinical results, I continue to relieve her by the persistent use of histaminase.

DR. LAWRENCE C. GOLDBERG, Cincinnati: I do not feel that histaminase is a cure-all for any of the allergic conditions. As I tried to emphasize, it may be a helpful adjunct but we know that allergic conditions are variable and change from time to time. There are many factors that have to be thought of. I think that Dr. Goodman to some extent misconstrued my feeling about this drug, because I still would like to emphasize that it does not cure allergic conditions as we find it at the present moment. But it may help, and, if so, I think it should be tried. The drug should be kept in an ice box where it can always be cold. Large doses should be given, one or two tablets every hour, so that the level is consistent with the amount of histamine-like substance which may be set off in the body.

VERTEBRAL FRACTURES AS A COMPLICATION OF CONVULSIONS

IN HYPOGLYCEMIC SHOCK AND METRAZOL THERAPY IN PSYCHIATRIC DISORDERS

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In a previous communication we presented the frequent complication of vertebral fractures in the course of metrazol therapy in psychiatric disorders.¹ At that time, in a roentgenographic study of fifty-one psychiatric patients who had received treatment with metrazol, twenty-two (43.1 per cent) manifested compression fractures of the vertebrae, most commonly in the mid-thoracic region, and in most instances the fractures of the vertebral bodies were multiple. Fragmentation and compression of the anterior portion of the upper surface of the body occurred frequently, while in about half the cases the fractures manifested themselves only by a slight forward displacement of a disklike fragment of the upper portion of the body. There was a higher incidence of fractures in female (sixteen) than in male (six) patients.

At the time of the first report it was indicated that a study was being made of the effect of keeping the patient on his side in an acutely flexed position, since it was felt that the force of sudden flexions of the spine, which may be the cause of the vertebral fractures, would thereby be reduced.

The present report is an extension of our previous studies and includes a roentgenographic survey of the following groups: (1) patients who manifested convulsions during the course of hypoglycemic shock therapy; (2) patients who had received both hypoglycemic shock and metrazol therapy, with convulsions occurring during the insulin shock; (3) patients who were placed in the position of acute flexion during the treatment with metrazol; (4) a control series of patients who received hypoglycemic shock therapy but who had no convulsions, and also an untreated group of patients whose spines were examined roentgenographically.

Sakel² describes two types of hypoglycemic shock: the "wet shock," during which the patient sweats profusely, grows somnolent and goes into deep coma, and the "dry shock," during which an epileptic attack occurs in the second or third hour of hypoglycemia. He states that the type of response cannot be predicted in advance and is independent of the size of the dose. Early in the work on hypoglycemic shock therapy there was a difference of opinion as to the therapeutic value of these convulsions. At first, when they occurred, the shock was immediately interrupted by intravenous dextrose. Later, Sakel³ clarified this point by stating that in the "dry shock" the epileptic seizure is not dangerous and one may wait a few minutes before terminating the hypo-

glycemia by nasal tube. However, if the epileptic seizure occurs in the fourth or fifth hour of hypoglycemia there is presented a very dangerous situation, and hypoglycemia must be terminated at once by intravenous dextrose. Recently Sakel⁴ has specified that metrazol may be used to produce convulsions during the hypoglycemia in certain types of resistant cases and emphasizes that the therapeutic value of epileptic seizures was recognized in certain cases from the beginning of the insulin shock treatment.

Plattner and Frölicher, as quoted by Thomas and Wilson,⁵ state that in their series of cases convulsions occurred in 7.7 per cent of comas of unresponsive cases but in only 3.2 per cent of comas of remitting cases. Young and his co-workers⁶ encountered convulsions in 16 per cent of patients treated with insulin. Malzberg⁷ in a statistical study of 1,039 insulin-treated patients from the various New York state hospitals, found that 394 patients (38 per cent) had convulsions ranging in number from one to eleven and over. Of these, 220 (55 per cent) were males and 174 (44 per cent) were females. A survey of the literature reveals no report of the occurrence of vertebral fractures in the course of

TABLE 1.—Vertebral Fractures in Patients Treated with Shock Therapy

Classification of Patients	Number of Patients		
	Male	Female	Total
Patients treated with insulin shock.....	89	84	173
Patients with insulin convulsions.....	40	22	62
(a) Early convulsions, 33	(63%)	(35%)	(30%)
(b) Late convulsions, 195			
Patients with convulsions treated with insulin alone.....	31	15	46
(a) Patients examined roentgenographically....	22	12	34
(b) Patients with vertebral fractures.....	6	1	7
			(20.5%)
Patients treated with both insulin and metrazol..	9	7	16
(a) Patients examined roentgenographically....	6	6	12
(b) Patients with vertebral fractures.....	1	2	3
Patients treated with metrazol in position of acute flexion.....	1	6	7
(a) Patients examined roentgenographically....	1	6	7
(b) Patients roentgenographed prior to treatment.....	1	3	4
(c) Patients with vertebral fractures.....	1	4	5

hypoglycemic shock therapy. Recently it was called to our attention that Stalker⁸ reported a case of vertebral compression fracture due to convulsions induced by triazol, the chemical composition of which resembles that of metrazol.

Up to the present time 173 patients have been treated at the Psychiatric Institute with hypoglycemic shock therapy, the greatest number of whom were schizophrenic. Of these, eighty-four were females and eighty-nine males. Convulsions varying from one to twenty in number occurred in sixty-two patients (36 per cent), of whom twenty-two (35 per cent) were females and forty (65 per cent) were males (table 2). The total number of convulsions in the series of insulin-treated patients was 228 and the average number was 3.6. Considering those convulsions which occur in the second and

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2. Sakel, Manfred: A New Treatment of Schizophrenia, *Am. J. Psychiat.* 93: 829-841 (Jan.) 1937.

3. Sakel, Manfred, in Discussion on Hypoglycemia Symposium, *Am. J. Psychiat.* 94: 181-182 (July) 1937.

4. Sakel, Manfred: The Pharmacological Shock Treatment of Schizophrenia, authorized translation by Joseph Wortis, Nervous and Mental Disease Monograph 62, New York, Nervous and Mental Disease Publishing Company, 1938.

5. Thomas, W. R., and Wilson, Isabel G. H.: Report on Cardiazol Treatment and on the Present Application of Hypoglycemic Shock Treatment in Schizophrenia, London, His Majesty's Stationery Office, 1938, p. 33.

6. Young, G. A.; Young, R. H., and Rouck, Louis: Experiences with the Hypoglycemic Shock Treatment of Schizophrenia, *Am. J. Psychiat.* 94: 159-170 (July) 1937.

7. Malzberg, Benjamin: Outcome of Insulin Treatment of One Thousand Patients with Dementia Praecox, *Psychiat. Quart.* 12: 528-553 (July) 1938.

8. Stalker, Harry: Double Vertebral Compression Fracture from Convulsion Therapy, *Lancet* 2: 1172-1173 (Nov. 19) 1938.

third hour of hypoglycemia as "early" and those occurring in the fourth and fifth hour as "late," there were thirty-three of the former type and 195 of the latter. Of the sixty-two insulin-treated patients manifesting convulsions during hypoglycemia, sixteen subsequently had a course of metrazol therapy. Consequently only

roentgenograms were obtained for twelve, six males and six females. Compression fractures of the vertebrae were found in three of these cases. In this group there were one male and two females.

With the hope of preventing compression fractures of the vertebrae in the course of metrazol therapy, we

TABLE 2.—Detailed Study of Patients Manifesting Convulsions and Vertebral Fractures in Hypoglycemic Shock and Metrazol Therapy

Case No.	Name	Age	Diagnosis	Number of Insulin Convulsions	Number of Metrazol Convulsions	X-Ray Report *
Female Patients						
1	F. S.	18	Schizophrenia, catatonic	6	Not treated †	Negative
2	R. K.	24	Schizophrenia, hebephrenic	2	Not treated	Negative
3	N. S.	27	Schizophrenia, hebephrenic	3	10	Negative
4	S. C.	19	Schizophrenia, catatonic	3	Not treated	Not available
5	G. Z.	26	Schizophrenia, catatonic	1	Not treated	Negative
6	M. Z.	24	Schizophrenia, hebephrenic	5	Not treated	Negative
7	C. J.	16	Schizophrenia, hebephrenic	2	Not treated	Not available
8	A. P.	48	Schizophrenia, paranoid	1	Not treated	Not available
9	F. M.	16	Psychoneurosis, obsessive compulsive	8	Not treated	Negative
10	T. K.	23	Schizophrenia, hebephrenic	11	Not treated	Negative
11	A. C.	22	Schizophrenia, paranoid	4	Not treated	T 4-5
12	S. M.	22	Schizophrenia, catatonic	2	Not treated	Negative
13	S. H.	35	Schizophrenia, catatonic	1	3	Negative after insulin; fracture T 5-6-7-8 after metrazol
14	A. K.	31	Schizophrenia, hebephrenic	3	Not treated	Negative
15	K. F.	29	Schizophrenia, catatonic	1	Not treated	Negative
16	F. J.	33	Schizophrenia, paranoid	1	5	Negative after insulin; negative after metrazol in position of hyperextension
17	B. K.	22	Schizophrenia, hebephrenic	8	22; combined insulin and metrazol 12	Negative
18	B. H.	30	Schizophrenia, paranoid	20	14	Not available
19	G. O.	17	Schizophrenia, catatonic	5	19	T 6-7-8
20	L. O.	25	Schizophrenia, mixed	5	3	T 7-8
21	M. G.	17	Schizophrenia, hebephrenic	2	5	Negative
22	S. B.	30	Manic-depressive, agitated depression	1	3	Negative
Male Patients						
23	N. M.	18	Schizophrenia, catatonic	3	18	T 4-5
24	G. S.	14	Schizophrenia, hebephrenic	2	15	Negative
25	L. S.	15	Schizophrenia, hebephrenic	5	Not treated	T 6-8
26	B. W.	17	Schizophrenia, catatonic	3	1	Negative
27	J. P.	15	Schizophrenia, hebephrenic	7	13	Not available
28	S. M.	23	Schizophrenia, catatonic	5	14	Negative
29	J. G.	26	Schizophrenia, hebephrenic	1	Not treated	Not available
30	J. F.	31	Schizophrenia, paranoid	1	Not treated	Negative
31	S. W.	15	Schizophrenia, hebephrenic	2	7	Negative
32	S. G.	34	Schizophrenia, paranoid	1	Not treated	Negative
33	J. Q.	40	Schizophrenia, paranoid	2	Not treated	Not available
34	L. G.	15	Schizophrenia, simple	3	Not treated	Negative
35	T. O.	22	Schizophrenia, hebephrenic	4	Not treated	T 5
36	A. M.	16	Schizophrenia, hebephrenic	2	Not treated	Not available
37	I. H.	33	Schizophrenia, hebephrenic	2	Not treated	Negative
38	L. B.	18	Schizophrenia, hebephrenic	6	Not treated	Not available
39	M. H.	18	Schizophrenia, hebephrenic	4	Not treated	T 4-5
40	J. M.	20	Schizophrenia, catatonic	7	22	Not available
41	J. C.	13	Schizophrenia, catatonic	3	9	Negative after insulin; fracture T 9-10-11 after metrazol
42	R. M.	21	No psychosis, epileptic personality	1	Not treated	Not available
43	D. G.	22	Schizophrenia, simple	1	Not treated	Not available
44	R. H.	20	Schizophrenia, hebephrenic	8	Not treated	Negative
45	M. S.	18	Schizophrenia, simple	2	Not treated	Negative
46	J. M.	23	Schizophrenia, hebephrenic	2	Not treated	Not available
47	C. S.	21	Schizophrenia, hebephrenic	3	Not treated	T 7
48	E. P.	19	Schizophrenia, hebephrenic	2	Not treated	Negative
49	M. M.	19	Schizophrenia, hebephrenic	5	Not treated	Negative
50	F. W.	33	Schizophrenia, hebephrenic	2	Not treated	T 6-7
51	L. H.	17	Schizophrenia, mixed	4	Not treated	Negative
52	T. S.	27	Manic-depressive, depressed	4	Not treated	T 6-7
53	M. D.	25	Schizophrenia, paranoid	1	Not treated	Not available
54	C. L.	27	Psychosis with chronic encephalitis	5	Not treated	Negative
55	H. J.	30	Schizophrenia, hebephrenic	1	16	Negative
56	J. F.	20	Schizophrenia, hebephrenic	2	Not treated	Negative
57	L. O.	18	Schizophrenia, catatonic	2	Not treated	Negative
58	H. B.	11	Schizophrenia, hebephrenic	5	Not treated	Negative
59	D. T.	5	Psychosis with mental deficiency	6	6	Not available
60	J. P.	8	Schizophrenia, hebephrenic	4	Not treated	Negative
61	M. M.	5	Psychosis with mental deficiency	8	Not treated	Negative
62	A. H.	3	Schizophrenia, undetermined	2	Not treated	Not available

* The letter T and the number represent a compression fracture of the corresponding thoracic vertebra. † Not treated with metrazol.

forty-six patients, fifteen females and thirty-one males, had convulsions during hypoglycemia without any other complicating therapy. Of these, thirty-four were available for roentgenographic study, twenty-two males and twelve females. Compression fractures of the vertebrae were observed in seven (20.5 per cent) patients, six males and one female. In six of these patients late convulsions had occurred.

Of the sixteen patients (nine males and seven females) who had both insulin and metrazol treatment,

have treated seven patients, six females and one male, in the position of acute flexion. Roentgenograms showing no abnormalities of the spine were obtained for four of these patients prior to treatment. After several metrazol-induced convulsions, five patients, four females and one male, showed compression fractures of the vertebrae (table 1).

It is noteworthy that two of these patients had previously had convulsions during a course of hypoglycemic shock and showed no fractures on roentgenographic

examination, whereas, after a few metrazol-induced convulsions were given compression fractures of the thoracic vertebrae were demonstrated.

As a control series we have used a group of twenty-eight patients, seven males and twenty-one females, who had roentgenograms of the thoracic spine. Twenty of these patients have received or are receiving insulin

On the thirty-second treatment day, with a dose of 110 units, his second convulsion developed at 11:10 a. m. A third convulsion occurred on the thirty-eighth day with a dose of 90 units, at noon. The fourth and last convulsion occurred at 11 a. m. on the forty-fifth day, with a dose of 80 units. In all, he had thirty-three comas, and hypoglycemic shock therapy was terminated December 6, the patient being much improved. He was discharged as recovered March 1, 1938.



Fig. 1 (case 52).—A white man aged 27 with a manic-depressive psychosis of the depressed type had four convulsions during the course of hypoglycemic shock therapy. A roentgenogram then revealed compression fractures of the sixth and seventh thoracic vertebrae.



Fig. 2 (case 39).—A white youth aged 18 with schizophrenia had four convulsions during the course of hypoglycemic shock therapy. A roentgenogram then revealed compression fractures of the fourth and fifth thoracic vertebrae.



Fig. 3 (case 23).—A youth of 18 with schizophrenia had four convulsions during hypoglycemic and eighteen during metrazol therapy. Compression fractures of the fourth and fifth thoracic vertebrae, with evidence of bone production over the anterior margins of both vertebrae, were revealed.

shock treatment, but in none of them have there been frank epileptoid convulsions, although ten have had tonic spasms, rigidity of the arms, severe twitchings, marked myoclonic movements and generalized tremors. Eight patients are newly admitted and have had routine roentgenograms of the spine. In none of these twenty-eight patients was there any evidence of injury to the thoracic vertebral bodies.

In treating patients with metrazol, we are now utilizing a position of hyperextension. The patient, lying supine, has an air cushion placed along the thoracolumbar region of the back. The metrazol injection is then given, and during the convulsion the spine is limited in activity as much as possible by nurses holding the shoulders and pelvis, but not too rigidly. Our experience has been too limited to pass any judgment as to the efficacy of this method.

It is probable that the fractures of the mid-dorsal vertebrae are due to sudden acute flexion of the spine. Since the extensor group of muscles of the spine are weakest in the mid-dorsal region, the vertebral column secures the least amount of protection against flexion in this area.

The fractures seen following insulin convulsions were similar in nature to those sustained following the use of metrazol. They were, however, less extensive, and as a rule fewer vertebrae were involved.

REPORT OF CASES

CASE 52.—T. S., a white man aged 27, married, was admitted to the Psychiatric Institute April 19, 1937, with a diagnosis of manic-depressive psychosis, depressed type, of nine months' duration. The patient was well nourished, of pyknic habitus, and showed no pathologic condition on physical or laboratory examination. Hypoglycemic shock therapy was instituted September 28. On the fifteenth day of treatment with a dose of 125 units of insulin, the patient reached coma at 11:30 a. m. and had an epileptoid convulsive seizure fifteen minutes later.

Approximately a year later, March 27, 1939, the patient was recalled for investigation, at which time stereoscopic roentgenograms revealed compression fractures of the sixth and seventh dorsal vertebrae. He had not at any time complained of back pain (fig. 1).

CASE 39.—M. H., a white youth aged 18, single, was admitted to the Psychiatric Institute March 14, 1938, with a diagnosis of dementia praecox, hebephrenic type, of one and one-half

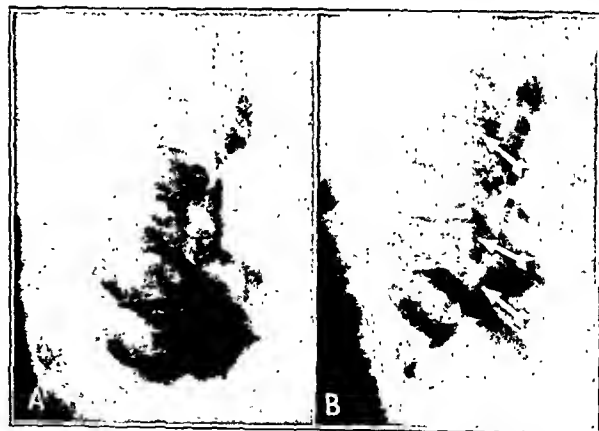


Fig. 4 (case 13).—A white woman aged 33 with schizophrenia had one convulsion during a course of hypoglycemic shock therapy. A roentgenogram (A) then revealed no abnormalities of the thoracic vertebrae. After three metrazol-induced convulsions a roentgenogram (B) revealed compression fractures of the fifth, sixth, seventh and eighth thoracic vertebrae. The patient had been placed in the position of acute flexion during treatment.

years' duration. He was well nourished, of asthenic habitus, and presented no pathologic changes on physical or laboratory study. He was placed on hypoglycemic shock therapy May 31. On the twenty-second treatment day, with a dose of 150 units of insulin, the patient had an epileptoid convulsive seizure at 9:25 a. m. On the twenty-eighth treatment day, with a dose

of 150 units, the second convulsion developed at 9:24 a. m. A third convulsion occurred on the thirty-first treatment day, with a dose of 120 units, at 9:20 a. m. The fourth and last convulsion occurred at 9:54 a. m. on the thirty-seventh treatment day, with a dose of 85 units. In all, the patient had twenty-eight comas, and hypoglycemic shock therapy was terminated July 22 because of fracture dislocation of the left humerus sustained during the last insulin convulsion. His mental condition was much improved and he was discharged from the hospital October 15.

During the course of this investigation the patient was requested to return to the hospital for stereoscopic roentgenograms, which were taken March 25, 1939. These revealed compression fractures and slight wedging of the bodies of the fourth and fifth dorsal vertebrae. Although the patient complained vehemently of pain in the left arm when it was fractured, there was no complaint of back pain (fig. 2).

CASE 23.—N. M., a white youth aged 18, single, was admitted to the Psychiatric Institute Dec. 22, 1933, with a diagnosis of dementia praecox, catatonic type, of three and one-half years' duration. He was thin and fairly well developed, of asthenic habitus, and showed no pathologic condition on physical or laboratory examination. He began hypoglycemic shock therapy Oct. 28, 1936. On the twenty-fourth treatment day, with a dose of 75 units of insulin, the patient had an epileptoid convulsive seizure at 11:50 a. m. A second convulsion occurred on the thirtieth treatment day, with a dose of 50 units, at 11:20 a. m. The third and last convulsion was observed at 11:25 a. m. on the seventy-sixth day of treatment, with a dose of 100 units. In all, the patient had twenty-nine comas, and insulin shock treatment was terminated Feb. 20, 1937, with no observable improvement in the condition.

Metrazol therapy was instituted April 13. The patient had eighteen grand mal seizures, and the maximum dose of metrazol was 6 cc. Treatment was discontinued July 2, the patient being unimproved.

He was removed from the hospital July 5, against advice, and was subsequently admitted to the Kings Park State Hospital, where roentgenograms were obtained April 12, 1939, for this study. These stereoscopic x-ray films showed compression fractures involving the fourth and fifth thoracic bodies, with evidence of bone production over the anterior margins of both vertebrae (fig. 3).

CASE 13.—S. H., a white woman aged 33, married, was admitted to the Psychiatric Institute April 16, 1937, with a diagnosis of dementia praecox, catatonic type, of seven months' duration. She was well nourished, of dysplastic habitus, with some evidence of hypothyroidism. There was no further pathologic physical or laboratory evidence. The patient had three courses of hypoglycemic shock therapy, the first course beginning May 10, 1937, and the last course terminating Dec. 28, 1938. She had improved after the first two courses but had relapsed after a short time. No convulsions occurred during the first two courses, but in the third course on the twelfth day of treatment, with a dose of 135 units of insulin, the patient had an epileptoid convulsion at 10:04 a. m. Stereoscopic roentgenograms of the dorsal spine taken March 22, 1939, revealed no evidence of fracture, injury or abnormality (fig. 4A). The patient manifested no improvement in her mental condition.

Metrazol therapy was instituted March 27, at which time the injection of 5 cc. of a 10 per cent solution of metrazol produced a generalized epileptoid convulsion. Similar convulsions were produced with the same dose March 29 and March 31. Stereoscopic x-ray films of the dorsal spine, taken March 29, revealed compression fractures of the fifth, sixth, seventh and eighth dorsal vertebrae (fig. 4B). During the metrazol treatment the patient was placed in the position of acute flexion, since it was thought that this position would minimize the possibility of fracture. Although she did not actually complain of backache, she was observed clutching her back as if in pain.

SUMMARY AND CONCLUSIONS

1. In a series of 173 patients treated with hypoglycemic shock therapy, sixty-two (36 per cent) manifested epileptoid convulsions.

2. The greatest number of convulsions occurred in the fourth or fifth hour of hypoglycemia.

3. Of thirty-four patients who received only hypoglycemic shock therapy and who were available for roentgenographic examination of the thoracic spine, 20.5 per cent revealed compression fractures of the vertebrae. The incidence was higher in male than in female patients.

4. Of twelve patients treated with both insulin and metrazol who were available for roentgenograms of the spine, three showed compression fractures of the vertebrae.

5. Maintaining the patient in the position of acute flexion while giving metrazol failed to prevent fractures.

6. Two patients with negative x-ray evidence following convulsions during insulin shock therapy subsequently showed compression fractures after metrazol-induced convulsions.

7. A control series of patients with no history of convulsions showed no evidence of injury to the vertebral bodies.

8. The effect of maintaining hyperextension of the spine during metrazol treatment is being investigated.

722 West One Hundred and Sixty-Eighth Street.

RECURRENT LYMPHOCYTIC CHORIOMENINGITIS TREATED WITH SULFANILAMIDE

ISOLATION OF VIRUS

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Lymphocytic choriomeningitis has been recognized as a distinct clinical entity for almost a half century. Wallgren¹ reviewed cases through 1924 and referred to this disease as "acute aseptic meningitis." In 1934 Abramson² reviewed cases up to that time. Toomey³ reported seventy cases in 1936. Dummer, Lyon and Stevenson⁴ reported twenty-two cases in 1937. There have also been reports by Gibbens,⁵ Gordon and Abrahams,⁶ Viets and Watts,⁷ Ashton,⁸ Mollaret and Kreis,⁹ Baird and Rivers,¹⁰ Rodier,¹¹ Rankin,¹² and

Dr. S. O. Levinson, of the Samuel Deutsch Serum Center, gave helpful suggestions and criticisms.

From the Cook County Contagious Hospital (Drs. Leichenger and Lack), the Department of Pediatrics, University of Illinois College of Medicine (Dr. Leichenger), and the Samuel Deutsch Serum Center, Michael Reese Hospital (Mr. Milzer).

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Ferru.¹³ All these reports emphasize the usual features that distinguish this entity. These are the benign course, the symptoms and signs of meningeal irritation, the spinal fluid features of pleocytosis, elevated protein content, and the absence of a bacterial agent. Only in the last five years has the virus nature of this disease been demonstrated by Armstrong and Lillie.¹⁴

Matturri-Matrai¹⁵ in 1937 reported the case of a 10 year old girl who had two distinct attacks of aseptic meningitis within a period of eighteen days. There was an interval of entire well-being between attacks which lasted eleven days.

In 1937 Cucco¹⁶ reported a case in which there were five distinct attacks over a period of three years. The Olmcs and Alliez¹⁷ reported a case which was characterized by a single recrudescence.

In these last three instances no attempt was made to isolate the etiologic agent or to show evidence that neutralizing antibodies were present in the patient's blood serum. In other words, the diagnosis rested entirely on clinical evidence. Skogland and Baker¹⁸ recently reviewed cases of lymphocytic choriomeningitis with sequelae. They reported a case characterized by signs and symptoms of chronic meningo-encephalitis lasting one and one-half years after the initial onset. Neutralizing antibodies were repeatedly demonstrated in the patient's blood. No mention is made, however, of any attempt to recover the virus.

before admission. Associated with these symptoms was repeated vomiting for four days prior to entrance to the hospital.

On admission physical examination revealed a temperature of 101.6 F. (rectal), pulse rate 68, respiratory rate 26 per minute and blood pressure 124 mm. of mercury systolic, 78 mm. diastolic. The positive observations were marked neck rigidity and positive Kernig and Brudzinski signs. Laboratory tests were all negative except that the spinal fluid had a ground glass appearance, a 4 plus Pandy reaction and 700 cells per cubic millimeter with 92 per cent lymphocytes. A direct smear and subsequent culture were negative for bacteria, as were results of guinea pig inoculation and special culture for tubercle bacilli. Spinal fluid and blood Wassermann and Kahn reactions were negative. The white cell count showed 12,200 cells per cubic millimeter, of which 68 per cent were of the polymorphonuclear type. The chest roentgenogram was essentially normal.

Our first impression was that we were dealing with tuberculous meningitis, but the subsequent course made this diagnosis untenable. At the Cook County Contagious Hospital all patients with meningitis of undetermined origin are placed on sulfanilamide until the type of meningitis is established. Consequently our patient received 15 grains (1 Gm.) every half hour for six doses and then 15 grains every four hours as a maintenance dose. In three days the temperature dropped to normal, and all objective signs and subjective symptoms disappeared.

Throughout the entire course of the illness, spinal punctures were performed at frequent intervals. The results are shown in the table. These data are fairly consistent. The fluid was

Spinal Fluid Study

	First Admission			Second Admission				Third Admission	
	Initial Attack			First Recurrence		Second Recurrence		Third Recurrence	Fourth Recurrence
Date.....	10/16/38	10/24/38	10/28/38	11/4/38	11/9/38	11/28/38	12/21/38	1/17/39	1/26/39
Color.....	Opalescent	Clear	Clear	Opalescent	Clear	Clear	Clear	Opalescent	Opalescent
Pandy reaction.....	4 plus	4 plus	1 plus	3 plus	2 plus	3 plus	3 plus	4 plus	4 plus
Total cells per cubic millimeter.....	700	110	70	860	80	235	76	970	846
Lymphocytes, per cent.....	92	76	96	61	99	70	97	90	103
Sugar, mg. per 100 cc.....	...	30	26	34	20
Protein, mg. per 100 cc.....	337	350
Chlorides, mg. per 100 cc.....	720	670	670	670
Culture and smear.....	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Wassermann and Kahn tests.....	Negative	Negative	Negative	Negative

We wish to report a case which we feel is unique in that it was characterized by an initial attack followed by four distinct recrudescences occurring over a period of four months. We also feel that we have adequately demonstrated the presence of the virus of lymphocytic choriomeningitis in the patient's spinal fluid. And finally, we wish to call attention to the fact that sulfanilamide was used in the treatment of this condition with apparent success.

REPORT OF CASE

First Admission.—Initial attack: J. P., a Negro aged 24, born in the United States, admitted to the Cook County Contagious Hospital Oct. 16, 1938, whose past history was of no significance, gave a history of a cough of one year's duration and some weakness, and loss of weight of one month's duration. Headache and stiff neck were present for two weeks

opalescent to clear and contained an increase in lymphocytes, the protein was elevated, and chlorides and sugar were at the lower levels of normal. Bacterial cultures, results of guinea pig inoculation for tubercle bacilli and the spinal fluid Wassermann reaction were all negative. The total cell count in the spinal fluid was markedly elevated with each recurrence.

The patient was discharged for the first time October 30, fourteen days after admission, clinically well. The discharge diagnosis was acute serous leptomeningitis.

Second Admission.—First Recurrence: November 4, five days after his first discharge, our patient was again admitted to the Contagious Hospital with the first recurrence. He gave a history of having been well until twenty-four hours before admission, at which time a severe frontal headache developed. Twelve hours later an elevated temperature and a stiff neck were noted. Physical examination at this time revealed a temperature of 104.6 F. The pharynx was slightly injected, neck rigidity was marked, and Kernig and Brudzinski signs were positive. Spinal puncture revealed essentially the same abnormal features that were noted previously and recorded in the table. The spinal fluid at this time contained 860 cells, of which 61 per cent were lymphocytes.

Immediately after admission the patient was placed on a regimen of 30 grains (2 Gm.) of sulfanilamide every four hours for five doses. This medication was repeated the next day, and on the third day the dose was reduced to 15 grains every four hours. At this time the concentration of sulfanilamide in the blood was 13 mg. per hundred cubic centimeters. The patient responded readily to treatment, becoming afebrile

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17. Olmer, D.; Olmer, Jean, and Alliez, J.: Méninçite aiguë lymphocytaire benigne a rechutes, Marseille-méd. 1: 683-686 (May 25) 1932.
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on the third day after admission, and on the fifth day the neck rigidity disappeared.

In the interim results of a complete work-up consisting of spinal fluid cultures, repeated blood culture, blood Wassermann test, agglutination tests for typhoid and undulant fever, test of the sedimentation time, x-ray study of the chest, urinalysis and complement fixation test for gonococci were negative.

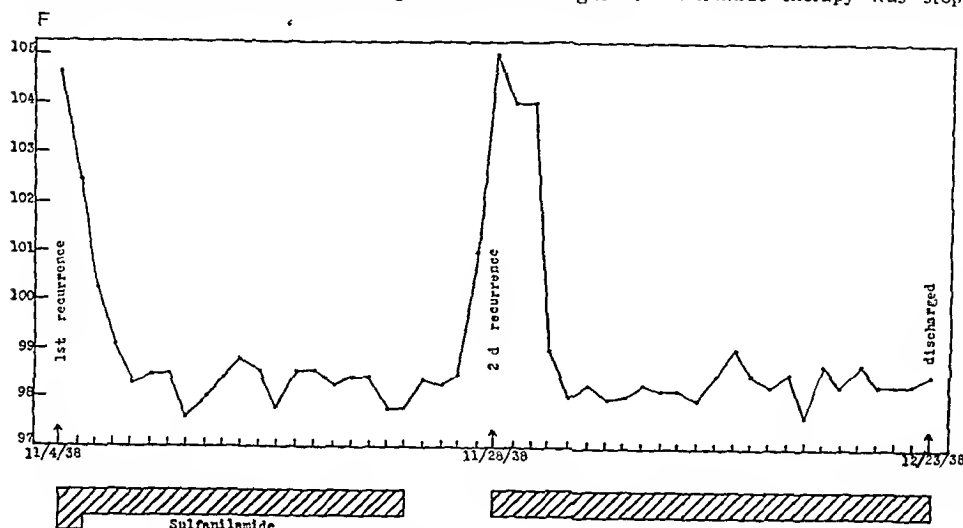


Chart 1.—Temperatures taken daily at 4 p. m. during the second admission.

November 23 sulfanilamide therapy was stopped because of the patient's excellent condition.

Second Recurrence: Five days later, November 28, the patient suddenly became acutely ill. The temperature rose to 105 F. (chart 1), he vomited several times and the stiff neck associated with other objective signs of meningeal irritation reappeared. Spinal puncture at this time showed 238 cells, 70 per cent of which were lymphocytes. Sulfanilamide therapy was reinstituted. In two days he became afebrile, and all physical features gradually became normal. The patient was released for the second time December 23, entirely asymptomatic; he was advised to continue taking 15 grains of sulfanilamide three times a day at home. He was discharged this time with a clinical diagnosis of recurrent lymphocytic choriomeningitis.

Third Admission.—Third Recurrence: This occurred Jan. 16, 1939. He had stopped taking sulfanilamide January 11, five days before admission. He was entirely well until two days before admission, when he noted an elevation in temperature, vomited a few times, became restless and irritable and had slight neck pains. Physical examination at the time of this admission showed a temperature of 102 F., the neck was rigid, and Kernig and Brudzinski signs were positive. The spinal fluid contained 970 cells per cubic millimeter with 90 per cent lymphocytes.

As previously, the patient was given 15 grains of sulfanilamide every four hours. The same satisfactory response was noted at once. Neck rigidity gradually disappeared, and the temperature returned to normal in four days. Five days after admission sulfanilamide medication was stopped.

Fourth Recurrence: Five days after discontinuance of sulfanilamide therapy symptoms again recurred. Neck rigidity developed for the fifth time. The temperature rose to 103 F., and this time there were 846 cells in the spinal fluid, practically all of which were lymphocytes. In order to see if the antipyretic action of sulfanilamide was responsible for the beneficial effects we substituted acetylsalicylic acid. This medication was continued for five days, but the patient's temperature remained elevated. Headache, vomiting, restlessness and neck rigidity persisted. Acetylsalicylic acid treatment was stopped, and sulfanilamide therapy was resumed. In three days all subjective symptoms and objective evidence disappeared (chart 2).

On February 13, seventeen weeks after the initial onset, our patient was entirely well. There were no evidences of any sequelae in the form of mental disturbances or localizing neuro-

logic features. He was discharged with a maintenance dose of $7\frac{1}{2}$ grains (0.5 Gm.) of sulfanilamide three times a day and was advised to report back to the hospital. One week later he reported no complaints and was told to continue the medication. He returned again March 4, feeling well. At this time his white count dropped to 5,100 cells per cubic millimeter. Sulfanilamide therapy was stopped. Our patient remained well and continued working until his last report to the hospital March 28, 1939, at which time contact with him was lost. Our final diagnosis was recurrent lymphocytic choriomeningitis.

ISOLATION OF THE VIRUS

Five cc. of cerebrospinal fluid collected from the patient at the onset of the fourth recrudescence (Jan. 26, 1939, thirteen weeks after the initial attack) were inoculated subcutaneously into guinea pig 3490. Five-tenths cc. which was seeded into aerobic and anaerobic culture mediums and incubated at 37 C. showed no bacteriologic growth after fourteen days.

In a previous publication¹⁹ one of the authors (A. M.) demonstrated that our stock of guinea pigs and white mice were free from latent infection with virus of lymphocytic choriomeningitis through repeated intracerebral inoculations with sterile starch, broth, and normal brain suspension. Furthermore, in the course of another study we had occasion to inoculate some fifty specimens of spinal fluid from various central nervous

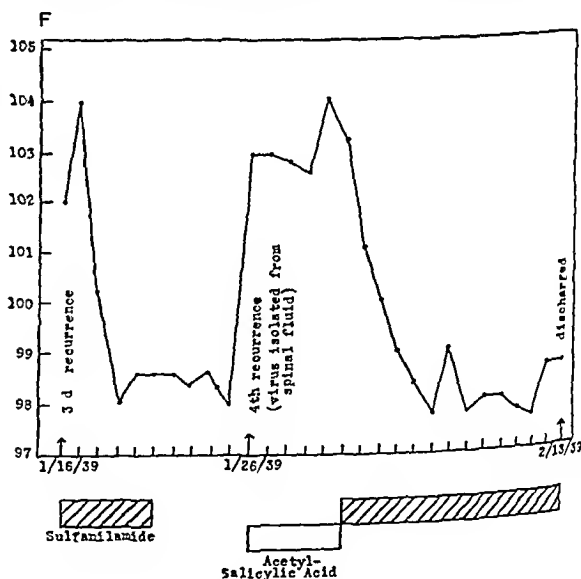


Chart 2.—Temperatures taken daily at 4 p. m. during the third admission.

system infections. Although all these specimens were inoculated in a routine manner subcutaneously into our guinea pigs and occasionally injected intracerebrally into our white mice, none of the animals developed lymphocytic choriomeningitis infection or immunity.

19. Shaughnessy, H. J., and Milzer, Albert: Experimental Infection of Dermacentor Andersoni Stiles with the Virus of Lymphocytic Choriomeningitis, *Am. J. Pub. Health* 29: 1103-1108 (Oct.) 1939.

We inoculate guinea pigs subcutaneously as a routine in addition to intracerebral inoculation of white mice for isolating the virus of lymphocytic choriomeningitis because (1) no one has reported activation of a latent infection of this virus by subcutaneous inoculation, and (2) the guinea pig may be readily infected by this route with many known strains. Moreover, we also found as did Traub²⁰ and Rivers and Scott²¹ that guinea pigs are equally susceptible to the intracerebral and the subcutaneous route with the same amounts of virus.

Inoculated guinea pig 3490 had a high temperature (104.2 F.) on the sixth day after inoculation and was found dead after eleven days. This animal had lost 75 Gm. in ten days. At autopsy the brain was intensely hyperemic and diffuse bronchopneumonia was present in the lungs. No bacteria were isolated from the brain tissues or heart's blood of this animal.

The brain was then removed aseptically, and a 10 per cent suspension by weight was prepared in buffered saline solution. Two cc. of this suspension was injected subcutaneously into guinea pig 3491, and 0.03 cc. was injected intracerebrally into each of six white mice. All six inoculated mice had rough coats and coarse body tremors on the sixth day after inoculation. Three of the mice were found dead with characteristic opisthotonos and rigid extension of the hind legs, on the seventh, seventh and eighth days respectively following inoculation. The other three mice recovered and were tested for immunity thirty days after the first inoculation by an intracerebral injection with 0.03 cc. of a 10 per cent suspension of W. E. (Rivers) strain of lymphocytic choriomeningitis virus. The surviving mice were immune to the W. E. strain of virus for the ensuing thirty days, while three control mice inoculated at the same time succumbed in eight days. Histologic examination of the brains of mice and guinea pigs that succumbed to our strain of virus revealed round cell infiltration of the meninges and choroid plexus identical with that produced by the W. E. strain of virus.

Guinea pig 3491 (second passage animal) had a high temperature (104.2 F.) twenty-four hours after the inoculation and was found dead after eight days. This animal had lost 40 Gm. in seven days. At autopsy the brain was hyperemic and other organs were grossly normal. No bacteria were isolated from the brain tissues or heart's blood of this animal.

Virus obtained from guinea pig 3491 was carried through two subsequent passages by further subcutaneous inoculation in guinea pigs. A neutralization test was then carried out using a slight modification of the technique described by Baird and Rivers.¹⁰ Guinea pig 3493 (fourth passage animal) was killed when moribund and its brain was removed aseptically; a 10 per cent suspension by weight in buffered saline solution was prepared and diluted serially to 10⁻⁵. Then 0.5 cc. of immune guinea pig lymphocytic choriomeningitis antiserum²² was mixed with each of the virus dilutions. At the same time control tubes were prepared using normal guinea pig serum plus virus. The mixtures of virus and serum were incubated at 37 C. for one hour. Five-tenths cc. of each dilution was injected subcutaneously into a guinea pig, and the animals were observed for thirty days. All of the guinea pigs which received the

immune serum-virus mixtures continued to gain weight, showed no temperature rise and survived, while the control guinea pigs which had received the normal serum-virus mixtures succumbed in nine to ten days with typical signs of lymphocytic choriomeningitis. This evidence that our strain is identical with other known American strains of lymphocytic choriomeningitis virus was confirmed by Dr. Thomas M. Rivers.²³

We maintained our virus by continued subcutaneous inoculations in guinea pigs. After the tenth passage a titration experiment was carried out to compare the infectivity of our strain with that of the W. E. strain in guinea pigs by subcutaneous inoculation (0.5 cc.) of dilutions ranging from 10⁻¹ to 10⁻⁶. The W. E. strain had also been maintained in our laboratory by subcutaneous inoculation; it had been passed for fifty-seven generations prior to the titration. Our strain after the tenth passage was decidedly less pathogenic for guinea pigs than the W. E. strain. The former killed in 10⁻⁴ dilutions, while the W. E. strain killed in 10⁻⁶ dilutions. A second titration experiment performed after our strain had been passed for twenty-eight generations gave evidence of increased pathogenicity, for at this time it also killed guinea pigs in 10⁻⁶ dilutions.

To date our strain has been passed for thirty-two generations. It is now 100 per cent fatal for guinea pigs when 0.5 cc. of a 10⁻⁴ dilution is inoculated subcutaneously. It also kills from 50 to 75 per cent of white mice when given by intracerebral inoculation (0.03 cc. of a 10 per cent suspension).

Filtration experiments have shown that our strain diluted in buffered saline solution (1/20) readily passes through Berkefeld N candles. The infectivity for guinea pigs and white mice has not decreased noticeably after storage for 210 days at 4 C. in a mixture of 9 parts 50 per cent glycerin and 1 part inactivated rabbit serum.

Serum obtained from the patient thirteen weeks after the initial attack was sent to Dr. Charles Armstrong, of the National Institute of Health, for the detection of lymphocytic choriomeningitis antibodies. He reported that he was unable to detect such neutralizing antibodies. A second specimen of serum obtained from the patient seventeen weeks after the onset of the disease (four weeks after the last attack) was sent to Dr. Thomas M. Rivers, who reported that the serum contained neither complement-fixing nor neutralizing antibodies against the virus of lymphocytic choriomeningitis. Unfortunately, we lost contact with our patient and were unable to secure subsequent blood specimens.

COMMENT

From a clinical standpoint our case is of interest for two reasons: first, because of the recurrences; and second, because of the prompt response to sulfanilamide.

The usual case of lymphocytic choriomeningitis is characterized by a single attack of meningeal irritation followed by prompt recovery. Our patient had four distinct recurrences in addition to the initial attack in a period of four months. We have already referred to the report by Skogland and Baker,¹⁶ who reviewed cases characterized by chronicity and neurologic sequelae. This would suggest that the entity of lymphocytic choriomeningitis is more variable in its course than was previously recognized.

The prompt response and apparent control of this malady by the use of sulfanilamide is of unusual interest. One gets the impression from the literature that sulfanilamide and its derivatives are of little value in the

20. Traub, Erich: An Epidemic in a Mouse Colony Due to the Virus of Acute Lymphocytic Choriomeningitis, *J. Exper. Med.* **63**: 533-546 (April) 1936.

21. Rivers, T. M., and Scott, T. F. McN.: Meningitis in Man Caused by a Filtrable Virus: II. Identification of the Etiological Agent, *J. Exper. Med.* **63**: 415-432 (March) 1936.

22. The lymphocytic choriomeningitis antiserum was furnished by Dr. Thomas M. Rivers, of the Rockefeller Institute for Medical Research.

23. Rivers, T. M.: Personal communication to the authors.

therapy of the human virus diseases. Rosenthal, Wooley and Bauer²⁴ found that although sulfanilamide and azo-sulfamide were ineffective, the original prontosil of Domagk (4-sulfonamide-2,4'-diamino-azobenzene) was effective in the early therapy of lymphocytic choriomeningitis in mice if large doses of the drug and small infective doses of the virus are employed. On the other hand, McKinley, Meck and Acree²⁵ inoculated mice with large infective doses of the virus and found that azosulfamide was ineffective. They also found that sulfanilamide and sodium sulfanilyl-sulfanilate were inactive against this virus infection.

This patient's course of illness under sulfanilamide is so unusual that we feel that the value of sulfanilamide in the treatment of lymphocytic choriomeningitis deserves further study.

Another unique feature of this case is the isolation of the virus of lymphocytic choriomeningitis from the cerebrospinal fluid thirteen weeks after the initial attack. MacCallum and Findlay²⁶ report a case in which the virus was still present in the nasopharynx twelve weeks after the onset but not demonstrable in the cerebrospinal fluid at the eighth week. Of course, it is not certain that the initial attack and all of the recrudescences in our patient were lymphocytic choriomeningitis, since no attempt was made to isolate virus prior to the fourth recurrence. However, the similarity of the initial attack and the four recrudescences, both from the laboratory and from the clinical picture, makes it very probable that they all arose from the same causative agent and were recrudescences of the same illness.

The failure to detect complement-fixing and neutralizing antibodies against the virus of lymphocytic choriomeningitis seventeen weeks after the onset of the disease and four weeks after the last recrudescence is not surprising in view of the recurrent course of this malady in our patient. Scott and Rivers²⁷ have stressed the slow development of antibodies in patients infected with this virus. Howard²⁸ has reported a case in which antibodies did not appear in the patient's serum for forty-five weeks after onset of the acute infection. More recently, MacCallum and Findlay²⁶ have reported that they failed to demonstrate neutralizing antibodies in specimens of serum collected from their patient on the ninth, twenty-fourth and fifty-eighth days after illness.

CONCLUSIONS

1. In a case of lymphocytic choriomeningitis lasting over a period of four months there were four distinct recrudescences following the initial attack.

2. Sulfanilamide therapy appeared effective in its control. Approximately 6,797 grains (453 Gm.) was given to this patient without ill effects.

3. The virus of lymphocytic choriomeningitis was isolated from the spinal fluid.

4. Neutralizing and complement-fixing antibodies were not detected in the patient's blood four weeks after the last recrudescence.

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24. Rosenthal, S. M.; Wooley, J. B., and Bauer, Hugo: *Studies in Chemotherapy: Chemotherapy of Choriomeningitis Virus Infection in Mice with Sulfonamide Compounds*, Pub. Health Rep. 52: 1211-1217 (Sept. 3) 1937.

25. McKinley, E. B.; Meck, J. S., and Acree, E. G.: *Chemotherapy in Virus Diseases*, J. Infect. Dis. 64: 36-42 (Jan.-Feb.) 1939.

26. MacCallum, F. O., and Findlay, G. M.: *Lymphocytic Choriomeningitis: Isolation of the Virus from the Nasopharynx*, Lancet 1: 1370-1378 (June 17) 1939.

27. Scott, T. F. McN., and Rivers, T. M.: *Meningitis in Man Caused by a Filtrable Virus: I. Two Cases and the Method of Obtaining a Virus from Their Spinal Fluids*, J. Exper. Med. 63: 397-414 (March) 1936.

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THE SYNTHETIC ESTROGEN STILBESTROL

CLINICAL AND EXPERIMENTAL STUDIES

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The estrogens in general use at present are estrone, estriol and estradiol, all of which are prepared primarily from pregnant mare's urine. These preparations are undeniably potent and clinically effective but have certain practical disadvantages: (a) They are expensive. (b) they are relatively ineffective orally and (c) they are difficult to prepare and, except when prepared in pure crystalline form, must be biologically standardized. A cheaper, orally effective, synthetic preparation which could be administered by weight is greatly to be desired.

The synthesis of a new estrogen which seemed to meet these criteria was announced by Dodds and his co-workers¹ in 1938. It was named diethylstilbestrol because it was derived from stilbene, contained two ethyl groups and was estrogenic. It does not contain the phenanthrene ring nucleus previously thought necessary for estrogenic activity. Preliminary animal studies revealed not only that it was approximately two and one half times as potent as estrone by injection but that it lost little of its potency when given by mouth. No toxic effects were noted in the early animal work.

Clinical trials of stilbestrol (the name adopted to designate diethylstilbestrol) have resulted in uniform agreement concerning its estrogenic effects but considerable disagreement concerning its toxicity. In Winterton and MacGregor's² series of fifty-one women, menopausal symptoms were relieved. Nausea was caused in only a few cases. Bishop, Boycott and Zuckerman³ obtained similar good effects, but three of their forty-three patients complained of nausea and vomiting. Varangot⁴ observed nausea and vomiting in eight of eighteen women. In this country preliminary reports on the clinical and toxic effects of the drug have been published by Shorr, Robinson and Papanicolaou,⁵ by Buxton and Engle⁶ and by us.⁷ Shorr and his co-workers found that thirty-five of forty-four women (80 per cent) had toxic symptoms in the form of nausea, vomiting, abdominal distress, anorexia, lassitude, paresthesias, vertigo, thirst, an acute psychotic reaction or cutaneous rashes. Liver function tests could not be considered conclusive but suggested hepatic impairment. The doses used ranged from 0.5 to 5 mg. daily, treatment being continued for from four to seventy-eight

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1. Dodds, E. C.; Goldberg, L.; Lawson, W., and Robinson, R.: *Estrogenic Activity of Certain Synthetic Compounds*, Nature, London 141: 247 (Feb. 5) 1938.

2. Winterton, W. R., and MacGregor, T. N.: *Clinical Observations with Stilbestrol*, J. Clin. Endocrinol. 1: 10 (Jan. 7) 1939.

3. Bishop, P., Boycott, J., and Zuckerman, S.: *Estrogenic Properties of Stilbestrol*, J. Clin. Endocrinol. 1: 10 (Jan. 7) 1939.

4. Varangot, J.: *Activité oestrogène et toxicité du stilbestrol* (4:4 dihydroxy alpha beta diethylstilbene), Presse méd. 38: 725 (May 13) 1939.

5. Shorr, Ephraim; Robinson, F. H., and Papanicolaou, G. N.: *A Clinical Study of the Synthetic Estrogen Stilbestrol*, J. A. M. A. 113: 2312-2318 (Dec. 23) 1939.

6. Buxton, C. L., and Engle, E. T.: *Effects of Diethylstilbestrol*, J. A. M. A. 113: 2318-2320 (Dec. 3) 1939.

7. MacBryde, C. M.; Freedman, Harold, and Loeffel, Ellen: *Studies on Stilbestrol*, J. A. M. A. 113: 2320 (Dec. 3) 1939.

days. Buxton and Engle found no evidence of toxicity in sixteen of seventeen cases. Albumin and casts were found in the urine in one case, possibly attributable to the drug. In our own series, as recorded in our preliminary report, nausea occurred in eight of thirty-seven patients, vomiting in three.

In this paper we propose to give a more complete report of our clinical and experimental studies of the effects of stilbestrol.^{7a}

CLINICAL MATERIAL AND METHODS

Studies were started in March 1939. Fifty-six women have been treated. Of these, fourteen have had both ovaries removed, nine have had part of the ovarian tissue removed, five were eunuchoid young women with amenorrhea and twenty-eight were suffering with symptoms of spontaneous menopause. Two criteria of selection of cases were employed: (1) symptoms severe and characteristic of hypo-ovarianism and (2) vaginal smears definitely of the inactive, castrate type. Patients have been given stilbestrol constantly for periods ranging from two weeks to eight months. Eighteen of the fifty-six have received stilbestrol constantly for six months or longer.

The dose has ranged from 0.1 to 5 mg. daily of stilbestrol dipropionate by mouth or intramuscularly in oil. The average dose has been 1 mg. daily and thirty-one of our patients are now maintained on this dose orally. The largest doses have been given two patients with primary hypogonadism. Each of them received slightly over 700 mg. intramuscularly in 180 days.

Vaginal smears were made at intervals, twice a week at first, later once a week and then once every two weeks. The dose necessary to obtain and maintain full estrous response was determined in each case. Subjective responses were analyzed as carefully as possible and an attempt was made to correlate the subjective and objective results and relate them to the dosage. Endometrial biopsies were made before and after treatment in eight cases.

On all patients receiving large doses over considerable periods of time, repeated tests of liver function, red blood cell and white blood cell counts, hemoglobin determinations, differential white cell counts and blood platelet counts were performed. Loeser⁸ has observed anorexia, vaginal and intestinal hemorrhage and liver cell degeneration in rats given large doses. Tislowitz⁹ found granulocytopenia and anemia in dogs receiving 5 mg. daily by injection for from twenty-five to fifty days. Morrell¹⁰ has shown no pathologic changes in tissues of rats, rabbits or monkeys. We¹¹ have found that both stilbestrol and natural estrogens in large dosage will produce anemia, thrombocytopenia and hemorrhage, as well as hypoplastic changes in the bone marrow of dogs.

In addition to the tests of liver function, repeated examinations of the urine have been done.

Two tests of liver function were used—bromsulphalein excretion and hippuric acid synthesis. In addition, the icterus index was determined at intervals and the prothrombin time measured.

7a. Stilbestrol for these studies was supplied to us by Dr. J. B. Rice, of the Medical Research Department, Winthrop Chemical Company.

8. Loeser, Arnold: Untersuchungen über die Pharmakologie und Toxikologie synthetischer Brunststoffe, *Ztschr. f. d. ges. exper. Med.* **105**: 430 (April) 1939; *Klin. Wchnschr.* **18**: 346 (March 11) 1939.

9. Tislowitz, R.: *Acta brev. Neerland* **9**: 15, 1939.

10. Morrell, J. A.: *Endocrinology*, to be published.

11. MacBryde, C. M.; Castrodale, Dante; Helwig, A. B.; Bierbaum, O., and Poe, J., to be published.

RESULTS

1. *Subjective Effects.*—Definite relief of hypogonadal symptoms was obtained in fifty-two of the fifty-six cases. The degree of relief varied from excellent in thirty-five cases to fair in seventeen cases. Hot flashes were decreased in all cases in which they were a prominent complaint. Headache was relieved in sixteen of twenty-one cases in which it had been severe. A tendency to nausea and vomiting was decreased in four cases. Energy seemed greater in twenty-eight of thirty-two patients who had complained of lassitude. Pruritus vulvae was relieved in eight of nine cases. Increased sexual desire was reported by twelve patients. These effects were in general similar to those we have previously seen with large doses (from 10,000 to 30,000 rat units weekly) of estradiol benzoate.

Untoward subjective effects occurred in nine of our fifty-six cases (16 per cent), consisting of slight nausea in five cases and of nausea and vomiting in four cases. In two of the four cases with vomiting the drug was later resumed, the dose being reduced from 5 mg. intramuscularly three times a week to 1 mg. by mouth daily, and nausea did not recur. In the other two cases the patients would not try the drug again.

No other untoward effects were observed. We had no patients who complained of abdominal distress or lassitude or who had cutaneous rashes or diarrhea.

2. *Objective Effects.*—The vaginal smears, which in all cases were of the inactive castrate type before treatment, showed active estrous changes under stilbestrol therapy. Within four days after 5 mg. intramuscularly the smears showed marked changes and in seven days the change was that of complete estrous response. After 1 mg. daily by injection the change was usually partial in seven days and complete in fourteen days. When given by mouth, 1 mg. daily takes on the average twenty-one days to cause the complete response.

After full vaginal smear changes were obtained at any dosage level and treatment was stopped, it took from twenty-one to thirty days for the smear to regress gradually to the castrate type. Symptomatic relief followed roughly the vaginal smear picture. Patients, however, frequently felt better before full estrus was reached and usually felt worse within one week after the drug was stopped, even though the vaginal smears might still appear quite active.

The endometrial biopsies revealed active proliferative changes after 10 mg. intramuscularly given in seven days, or after 20 mg. orally in fourteen days.

From the subjective and objective effects on our patients, stilbestrol would seem to be from 50 to 66 per cent as effective by mouth as by injection. The oral route seems more apt to cause nausea in susceptible patients but otherwise seems the route of choice.

Stilbestrol is considerably more active than estrone (theelin), the most widely used of the estrogens. A number of our patients had previously been treated with estrone, and some of them have since received courses of estrone for comparison with the stilbestrol effect. It is necessary to compare the same patient when making such a parallel study, a point which is evident when it is found that complete symptomatic relief and estrous changes were brought about in two cases only after 5 mg. daily by injection for approximately fourteen days, while at the other extreme 1 mg. daily by mouth has maintained a positive smear in several cases for months. In one case of a menopausal patient in which such a comparison can be made, 1 mg. of estrone (10,000

international units) three times a week by intramuscular injection was more than equaled objectively and subjectively by 0.5 mg. of stilbestrol daily by mouth. A patient with primary hypogonadism showed regression of smears and breast atrophy when given less than 1 mg. (10,000 international units) of estrone daily. Stilbestrol, 1 mg. by injection three times a week, caused breast growth and active vaginal changes. From these observations it would seem that stilbestrol dipropionate is more than twice as active per milligram as estrone when given intramuscularly and that a milligram of stilbestrol orally is approximately equivalent to a milligram of estrone by injection.

As compared with estradiol benzoate, similar observations in four cases have led us to conclude that stilbestrol is approximately one third to one half as potent when given by intramuscular injection.

An effective way to administer stilbestrol is by subcutaneous implantation of hard pellets of the pure crystalline drug, as we have described.¹² By extracting and weighing such pellets at intervals, a pellet of approximately 100 mg. is found to be absorbed at a rate ranging from 0.127 to 0.250 mg. a day. Symptomatic improvement and positive changes in the vaginal smears have been maintained for from four to seven months by eight castrate patients in whom one pellet has been implanted. Whether or not continuous therapy in such small doses by pellet implantation is preferable to oral therapy with larger doses, which can however be interrupted at intervals, is not yet determined.

All of our patients with small breasts receiving large doses of stilbestrol had breast growth of a degree sufficient to be measurable. Larger doses are required to produce progressive breast growth than are necessary to maintain estrous changes in the vaginal smear. Other patients noticed some sensitivity and tenseness of the breasts, with enlargement of the nipples and pigmentation of the areolae.

Uterine bleeding was produced in fourteen of the fifty-six cases. In ten of the fourteen cases this bleeding occurred after discontinuance of the drug, beginning from four to ten days later and lasting from three to fourteen days. In the remaining four cases bleeding started during treatment with the drug. Treatment was stopped in each case a few days after the bleeding started. In one case it lasted eight days, in one eleven days, in one twenty-three days and in one thirty-two days. In the last two cases cessation followed injections of progesterone. Endometrial biopsy showed a hypertrophic endometrium in the last case.

STUDIES OF TOXICITY

1. *Liver Function Studies.*—Twenty-six patients who had received the largest doses and had been treated for the longest periods had liver function studies performed, both by the bromsulphalein excretion and by the hippuric acid synthesis test. In six cases the tests were performed before any treatment was given and again after periods of from thirty to ninety days, during which amounts varying from 30 to 250 mg. had been given. The average daily dose in this group was 2 mg. daily, the minimum 1 mg. daily. In no case was there any significant change by either of the liver function tests.

In twenty cases the studies were not performed before the drug was started but after stilbestrol had been given for some time. Totals of from 120 to 700 mg. had been given in from 120 to 180 days. Bromsulphalein excretion and hippuric acid synthesis were well within normal limits in all these cases.

tion and hippuric acid synthesis were well within normal limits in all these cases.

Icterus index determinations were normal in all nineteen cases in which they were done and did not rise during continuous stilbestrol therapy.

2. *Blood Studies.*—No abnormalities were noted in total red blood cell counts, white blood cell counts, differential counts or platelet counts. No tendency to hemorrhage was observed in the skin or mucous membranes. The only bleeding produced was the uterine bleeding previously described. In none of the cases of prolonged bleeding was any abnormality of the blood noted except in the case in which the longest period of bleeding occurred. Here there was a slight fall in the red blood cell count and hemoglobin content, which returned to normal within two weeks after the bleeding ceased.

3. *Urine Studies.*—No urinary abnormalities occurred in twenty-two cases in which repeated urine examinations were made while under treatment for from two to eight months.

COMMENT AND SUMMARY

We have endeavored to judge the therapeutic and toxic effects of stilbestrol dipropionate when administered to fifty-six women suffering from severe hypogonadism. The results from the therapeutic standpoint are excellent, great relief of the symptoms of primary hypogonadism, of castration and of the menopause being obtained by thirty-five of fifty-six patients (62 per cent) and fair or partial relief by seventeen (30 per cent).

Nine patients (16 per cent) had unpleasant effects such as nausea and vomiting. The nausea occurred after injection therapy as well as after oral administration and cannot be considered due to direct gastrointestinal irritation. Reducing the dose or changing from oral to injection treatment reduces the tendency to nausea and was successful in all but two of our cases. In these two the stilbestrol treatment was discontinued.

It is important to determine whether the nausea and vomiting are evidence of more serious functional or organic disturbance or whether they may be considered relatively innocuous. Previous studies, both clinical and experimental, have given widely divergent results. Our results, as compared with those of Shorr, Robinson and Papanicolaou, show a much smaller percentage of untoward effects. Although the liver function studies which we performed showed no reason to suspect liver damage from the dosage employed, too much reliance cannot be put on such functional tests, as it is well known that minor hepatic impairment may be present without significant alteration.

Studies in our own laboratories¹¹ have shown that in dogs and rats receiving stilbestrol in doses comparable to the very highest therapeutic doses anemia and thrombocytopenia result. In animals receiving much larger doses, severe thrombocytopenia with hemorrhages and death may occur. However, we have also demonstrated similar results with comparable doses of estradiol benzoate, so that at present it seems doubtful whether in this respect there is any difference between the toxic effects of natural and of synthetic estrogens.

CONCLUSIONS

1. Stilbestrol dipropionate gave excellent subjective relief to thirty-five of fifty-six hypogonad women (62 per cent) and partial relief to seventeen (30 per cent).

2. It is a highly potent estrogen, producing estrous vaginal smears, proliferative changes in the endometrium, breast growth and all the other known effects of natural estrogens.

12. MacBryde, C. M.; Freedman, Harold; Loeffel, Ellen, and Allen, Duff: Estrogenic Therapy by Implantation of Stilbestrol Pellets, *Proc. Soc. Exper. Biol. & Med.* 43: 212-214 (Jan.) 1949.

3. Compared to estrone, stilbestrol is approximately twice as potent when given intramuscularly. A milligram of stilbestrol orally is roughly equivalent to a milligram of estrone intramuscularly.

4. By intramuscular injection, stilbestrol is approximately one third to one half as potent per milligram as estradiol benzoate.

5. Stilbestrol is roughly from 50 to 66 per cent as potent orally as by injection.

6. Nine patients (16 per cent) had unpleasant effects, consisting of nausea in five instances and of nausea and vomiting in four. In only two cases was it necessary to discontinue the drug. In no case were serious results detected. No abdominal distress, diarrhea or cutaneous rashes occurred.

7. Studies of liver function showed no evidence of hepatic impairment. No changes were noted in the blood or urine.

8. Further studies of stilbestrol and related compounds are indicated before these substances are released for general use. The toxic effects of the natural and of the synthetic estrogens should be compared, since it has been demonstrated that in high dosage both may be toxic.

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TESTICULAR TUMORS IN MICE RECEIVING ESTROGENS

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During the course of prolonged high estrogen treatment the glandular interstitial tissue of the testis in mice of the Strong A strain has been observed to hypertrophy, in a few instances to such an extent that large areas of the testis were composed entirely of these cells.¹ Since neither local invasions nor metastases were observed, not one of these hypertrophies or overgrowths was considered malignant. Recently, however, a malignant tumor of the interstitial cells appeared in an A strain mouse receiving estradiol benzoate.

This mouse had received weekly subcutaneous injections of 0.05 mg. of estradiol benzoate² in sesame oil beginning at the age of 30 days. Shortly after six months of treatment the left testis began to increase in size rather rapidly, and after eight months it was several times normal size, was nodular and protruded somewhat above the base of the tail. Shortly thereafter the general health of the animal appeared to decline, and it was killed for study 264 days after the start of treatment.

As shown in figure 1, the left testis was much enlarged, weighing 1.03 Gm.; it was brown and irregularly spherical. The tunica albuginea exhibited surface irregularities, and the epididymis was distorted and firmly adhered to the tunica. Microscopically this testis contained only an occasional remnant of a tubule and was composed almost entirely of cords and masses of large vacuolated cells resembling the hypertrophied

interstitial cells previously described¹ (fig. 2). Many of these cells were atypical in that they were multinucleated or contained finely granular basophilic nuclear inclusions. Although fat stains were not employed, the vacuolated character of the cytoplasm indicated a high lipid content. Mitotic figures were frequently encountered in these tumor cells. The tunica albuginea was extensively invaded and in places almost obliterated. The few remaining tubules were atrophic, the least degenerated of them containing Sertoli cells and spermatogonia or only Sertoli cells. Other tubules were entirely empty and frequently were represented only by sinusoid-like spaces.

The lumbar lymph nodes were greatly enlarged, as shown in figure 1, and the left node was the color of the left testis. The metastatic involvement of this node was so extensive that its lymphoid structure was lost, its chief component being the large vacuolated cells characteristic of the primary testicular lesion (fig. 3). The right lumbar node was normal in color and the metastatic involvement was limited primarily to the peripheral sinuses. A left renal node was similarly enlarged, brown, and infiltrated much the same as the left lumbar node. No other metastases were seen.

The right testis (weight 0.175 Gm.) was of normal shape and, although distinctly enlarged, it was much smaller than the left testis. It also was composed chiefly of large vacuolated interstitial cells which widely separated the tubules. The histologic features of this testis indicated the existence

of a marked diffuse hyperplasia which did not, in our opinion, represent a metastasis from the other testis. The tubules of the right testis were less severely damaged than those of the left and occasionally contained spermatocytes.

The accessory organs of reproduction, as is usual in estrogen-treated mice, exhibited increase in their fibromuscular tissue components. The extent of the expected estrogen effect was modified, however. The seminal vesicles were approximately two-thirds normal size, contained some secretion and were lined by a tall columnar epithelium almost identical with that of an untreated male or of a male receiving androgens. The lining epithelium of the coagulating glands was columnar rather than stratified squamous as usually seen after treatment with estrogens. The prostatic epithelium was essentially normal, as was the epithelium of the ejaculatory ducts and the prostatic urethra. The myxomatous

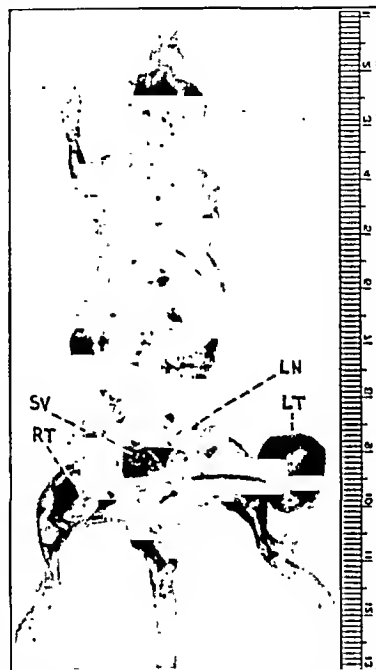


Fig. 1.—Mouse which received estradiol benzoate. The tumor of the left testis (LT) is 1.4 cm. in diameter and nodular. The right testis (RT) is hypertrophied, but to a lesser extent. The seminal vesicles (SV) are approximately two-thirds normal size. The lumbar lymph nodes (LN) are greatly enlarged.

From the Department of Anatomy, Yale University School of Medicine. This study was aided by grants from the Fluid Research Fund of Yale University School of Medicine, the Anna Fuller Fund, the Jane Coffin Childs Memorial Fund for Medical Research, and the Committee for Research in Problems of Sex of the National Research Council.
1. Gardner, W. U.: Hypertrophy of Interstitial Cells in the Testes of Mice Receiving Estrogenic Hormones, *Anat. Rec.* 68: 339 (June) 1937.
2. The estradiol benzoate was supplied by the Schering Corporation through Drs. E. Schwenk and Max Gilbert.

changes of the connective tissue of the ejaculatory ducts characteristically elicited by estrogen were lacking. The observations indicate that these tissues were under the influence of androgen, suggesting the possibility of endocrine activity of the hypertrophied and malignant cells.

Various abnormalities, usually seen in estrogen-treated mice,³ were also present in this animal. The bladder was greatly distended, the ureters and renal pelvises were dilated and the kidneys were enlarged. The bile ducts were modified, and the marrow cavities of the long bones were obliterated by endosteal deposits of new bone. The pubic symphysis was replaced by a ligament 1 mm. in length. The adrenals and the hypophysis, however, appeared normal.

A large tumor of the glandular interstitial cells also developed in one mouse of the A strain which received 250 micrograms of stilbestrol⁴ weekly from the thirty-sixth to the two hundred and eightieth day of life. This tumor was slightly smaller, measuring 10 mm. in diameter, but was almost identical histologically (fig. 4) with the tumor already described. No metastases were

The sequence of changes in the testis recalls that seen in the mammary glands, cervix uteri and hypophysis of estrogen-treated mice⁶ in that it consists of a hypertrophy of the affected element (in this case the interstitial cells) by increase in both size and number

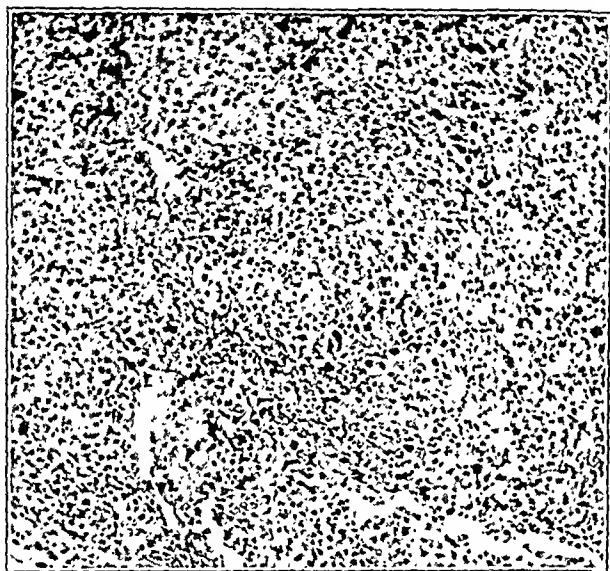


Fig. 2.—Section of an area of the testicular tumor of the mouse shown in figure 1; $\times 110$.

discovered, however, and its malignancy is unproved. The other testis of this animal again showed marked interstitial cell hypertrophy and the accessory genital organs manifested signs of androgen stimulation similar to those enumerated for the other animal.

Thus far, testicular tumors have not been observed in this laboratory to arise spontaneously in mice of the A strain, although the number of old males examined has perhaps been too small definitely to exclude the possibility of rare spontaneous origin. Moreover, tumors of the testis have not appeared in mice of other inbred strains receiving estrogens. Indeed, only mice of the A strain have responded to estrogens with interstitial cell hypertrophy.¹ Burrows,⁵ however, has reported rather a high incidence of Leydig cell hypertrophy in stock mice receiving estrogens.

3. Allen, E.; Hisaw, F. L., and Gardner, W. U.: *The Endocrine Functions of the Ovaries*, chapter VIII in Allen, Edgar; Danforth, C. H., and Doisy, E. A.: *Sex and Internal Secretions*, Baltimore, Williams & Wilkins, 1939.

4. The stilbestrol was supplied by E. R. Squibb & Sons through Dr. J. A. Morrell.

5. Burrows, Harold: A Comparison of the Changes Induced by Some Pure Estrogenic Compounds in the Mammary and Testes of Mice, *J. Path. & Bact.* 42: 161 (Jan.) 1936; Acquired Resistance to Estrone in a Male Mouse, *ibid.* 44: 699 (May) 1937.



Fig. 3.—Section of the metastasis of the testicular tumor to a lumbar lymph node; $\times 195$.

of cells followed by diffuse hyperplasia and finally malignancy. The testicular changes bear further general resemblance to the changes in the mammary glands, cervix and hypophysis in their appearance following chemically different estrogens and in their limitation by factors inherent in the strain of mice.



Fig. 4.—Section of the testicular tumor of the mouse receiving stilbestrol; $\times 100$.

SUMMARY

A large interstitial cell tumor of the testis which metastasized to the lumbar and renal lymph nodes developed in a mouse of the A strain receiving estradiol benzoate over a period of 264 days. A histologically

6. Gardner, W. U.: Estrogens in Carcinogenesis, *Arch. Path.* 27: 138 (Jan.) 1939. Lacassagne, A.: Les rapports entre les hormones sexuelles et la formation du cancer, *Ergebn. d. Vitamin- u. Hormonforsch.* 2: 259, 1939.

similar testicular tumor which did not metastasize also arose in a second mouse of the same strain receiving stilbestrol. The histologic picture of the accessory organs of reproduction in both instances indicates that these tumors secreted androgenic material.

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Clinical Notes, Suggestions and New Instruments

CHRONIC CONJUNCTIVITIS DUE TO THE VIRUS OF VENEREAL LYMPHOGRANULOMA

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Under the name Parinaud's conjunctivitis a peculiar inflammation of the conjunctiva of one eye with subsequent swelling of the regional preauricular and submaxillary lymph glands has been described. The various organisms that have been accused as possible causative agents include the tubercle bacillus (human and bovine), *Bacterium tularensis*, *Spirochaeta pallida*, the glanders bacillus, *Sporothrix*, *Streptococcus* and *Leptothrix*. The virus of venereal lymphogranuloma has also been listed among the etiologic organisms.

In this paper we are adding to the small number of recorded cases another case of conjunctivitis due to the virus of venereal lymphogranuloma.

The French ophthalmologist Morax¹ was the first author to call attention to the etiologic relationship of the virus of venereal lymphogranuloma to some cases of Parinaud's conjunctivitis, although he had no case of his own to prove his point. In the case of Levaditi, Bollack, Basch and Desvignes,² marked unilateral conjunctivitis of the bulb and lids and swelling of the preauricular and submaxillary glands occurred in a man aged 37. Material from an extirpated lymph node of the patient inoculated intracerebrally into a monkey produced a characteristic meningitis. Changes compatible with venereal lymphogranuloma were also evoked in mice by injection of the monkey brain emulsion. Further subpassages into mice were not successful. Frei tests with emulsions of the monkey and mouse brains as well as material from the preauricular glands of the patient gave positive reactions. Another case was that occurring in a woman physician³ at the Institute of Bacteriology of Louvain, Belgium, who had worked with the virus. Unilateral conjunctivitis and later preauricular and submaxillary lymphadenitis and parotitis with fever developed. The Frei reaction was positive. Causes other than venereal lymphogranuloma could be ruled out.

Similar involvement of the regional lymph nodes developed in Ichijo's⁴ case of unilateral conjunctivitis. In his and in Weidman's⁵ case, in which conjunctivitis was characterized by marked edema, genital manifestations of venereal lymphogranuloma preceded the involvement of one eye.

Experimentally, successful inoculations of the virus of venereal lymphogranuloma into the conjunctiva of chimpanzees with production of a characteristic conjunctivitis were performed by Levaditi, Schoen and Reinić.⁶

REPORT OF CASE

C. G., a white man aged 39,⁷ was presented at the December 1938 meeting of the New York Academy of Medicine, section

of Dermatology, with the diagnosis of chronic conjunctivitis of the right eye, probably due to the virus of venereal lymphogranuloma. This diagnosis has been confirmed by further study.

In 1926 the patient had gonorrhea which did not involve his eyes. In 1930 he had a generalized rash of secondary syphilis, the Wassermann reaction being 4 plus. At that time and subsequently he received adequate treatment with the arsphenamines, heavy metals and large doses of potassium iodide. This management led to a negative Wassermann reaction of the blood and to absence of signs and symptoms of syphilis but did not in the least influence a condition of the right eye which had developed during May 1932 and has persisted ever since. In 1935 he was operated on for anal fistula at Bellevue Hospital. At that time the clinical appearance of the rectum was not suggestive of venereal lymphogranuloma. A Frei test was not performed.

In May 1932, after perverted intercourse with a Negress, conjunctivitis of the right eye developed. The right preauricular and submaxillary nodes became swollen and tender. Agglutination tests for *Bacterium tularensis* were done twice and were negative. Tuberculin tests with dilutions of 1:100,000 and 1:10,000 gave negative results. Guinea pigs injected with macerated tissue from the conjunctiva remained well after eight days. Cultures of material from the eye yielded staphylococci or *Bacillus xerosis* or were sterile. A specimen of the eye was taken for biopsy on which the diagnosis was chronic granu-



Fig. 1.—Conjunctivitis of right eye in November 1938.

loma. In December 1932 the patient was presented by Dr. Abraham Fine⁸ before the Section of Ophthalmology of the New York Academy of Medicine. No definite diagnosis of the condition of the eye was made at that time. Until 1933, treatment at various times had consisted of injections with milk, roentgen and radium irradiation and topical applications, all without result. No more treatment was then attempted until 1938.

When seen at the Vanderbilt Clinic in November 1938, the right eye showed swelling and inflammation of both lids, with considerable edema, especially of the lower lid, and some purulent conjunctival discharge. There was marked destruction of the inner surface of the lids. The right globe was intensely injected. The cornea was opaque (fig. 1). Vision had been lost since 1933. At no time did the patient complain of pain in the eye.

There was no longer enlargement of any of the lymph nodes. General examination revealed no abnormality, and there were no signs of past or present venereal disease visible on the genitals or in the inguinal areas. Proctologic examination revealed a scar from an operation for anal fistula. In the opinion of the proctologist (Dr. C. V. Burt) there was nothing present to suggest venereal lymphogranuloma of the rectum.

Repeated Frei tests with reliable human antigens were strongly positive. A cutaneous test for elancroid (Ducrey's bacillus vaccine, Lederle) was doubtful (0.4 cm. slightly infiltrated redness).

8. Fine, Abraham: An Obscure Disease of the Conjunctiva Simulating Parinaud's Conjunctivitis, *Arch. Ophthalm.* 9: 677 (April) 1933.

From the Department of Dermatology and the Department of Bacteriology, Columbia University College of Physicians and Surgeons.

1. Morax, V., cited by Bollack, J.: *Bull. soc. franç. de dermat. et syph.* 43: 1243 (June) 1936.

2. Levaditi, C.; Bollack, J.; Basch, G., and Desvignes, P.: *Bull. soc. franç. de dermat. et syph.* 43: 1238 (June) 1936.

3. Ronse, Marguerite: *Ann. de la soc. belge de médecine tropicale* 18: 639 (Dec. 31) 1938. Bollack, J.; Basch, G., and Desvignes, P.: *Bull. soc. ophth.* 5: 409, 1936.

4. Ichijo, Morimasa: *Act. soc. ophth. Jap.* 41: 628 and 1487, 1937.

5. Weidman, F. D., in discussion of Weidman, F. D., and Hunter, Robert: *Lymphogranuloma Inguinalis*, *Arch. Dermat. & Syph.* 34: 342 (Aug.) 1936.

6. Levaditi, C.; Schoen, Rachel, and Reinić, Louis: *Compt. rend. Acad. d. sc.* 203: 828 (Oct. 26) 1936.

7. Hopkins, J. G.: *Chronic Conjunctivitis of the Right Eye, Probably Due to the Virus of Lymphogranuloma Venereum*, *Arch. Dermat. & Syph.* 39: 742 (April) 1939.

The serum protein value was 7.4 per cent, albumin 4.7 per cent and globulin 2.7 per cent.

Biopsy of the lid (Jan. 17, 1939) showed a fragment of conjunctival epithelium which in areas was infiltrated with polymorphonuclear cells. The major portion of the specimen was made up of very vascular granulation tissue. The numerous blood vessels were separated by masses of cells which were almost exclusively plasma cells. In places these were densely packed, in others separated by edema. In the latter areas there was considerable admixture of polymorphonuclear neutrophils. The walls of many of the small vessels were edematous and infiltrated with neutrophils. Many eosinophils and neutrophils

Results of Cutaneous Tests with Various Materials
Prepared as Antigens

Material	Cutaneous Reactions in Known Cases of Venereal Lympho- granuloma with Previous Positive Frei Tests (Human Antigens)	Cutaneous Reac- tions in Control Cases with Previous Negative Frei Tests (Human Antigens)
A. Filtered washings of eye...	—	—
	—	—
B. Tissue culture (inoculated with A unheated)	+	—
	+	—
	+	—
C. Tissue culture control.....	—	—
	—	—
D. Brain of mouse inoculated from tissue culture	+	—
E. Biopsy from eye *.....	+	—
	+	—
	+	—

* When injected previous to heating into monkey, produced transitory symptoms and cerebral changes, verified microscopically.

were seen in the lumen of the vessels. No definite diagnosis as to the nature of the granuloma was possible.

Four intravenous injections of Frei antigen were given without definite effect on the lesion of the eye. The first two injections caused systemic febrile reactions. The patient was then

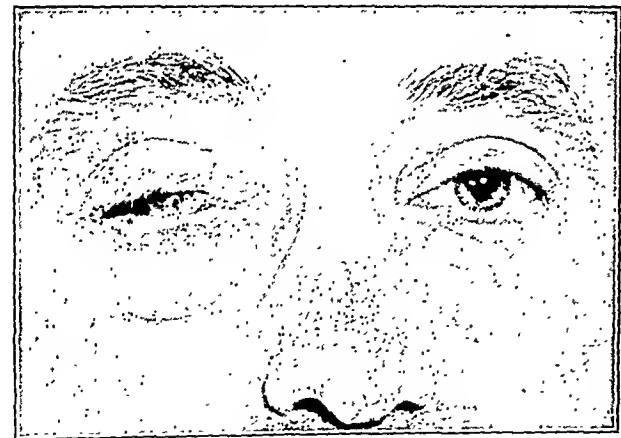


Fig. 2.—Right eye in April 1939 after treatment with sulfanilamide.

given sulfanilamide in doses of 80 and 60 grains (5 and 4 Gm.) a day. After a total of 540 grains (32.4 Gm.) less infiltration of the eyelids was noted. After continued treatment with sulfanilamide, which he took irregularly for four months, improvement of the eye progressed to a relatively satisfactory state (fig. 2). Five months after discontinuance of the drug Dr. Thygeson, the ophthalmologic consultant, stated "There is no evidence of ocular activity at present. The lids are adherent to the globe. The cornea is keratinized. There is no discharge. The eye feels comfortable. No surgery is advised."

EXPERIMENTAL WORK

Nov. 21, 1938, the conjunctival surfaces of the right eye were thoroughly irrigated with a buffered salt solution and the washings filtered through a Berkefeld V candle. Part of the filtrate was prepared as a Frei antigen. This gave no reaction on intradermal tests in three cases of lymphogranuloma (A in the table) as well as in control cases. Five drops of the unheated

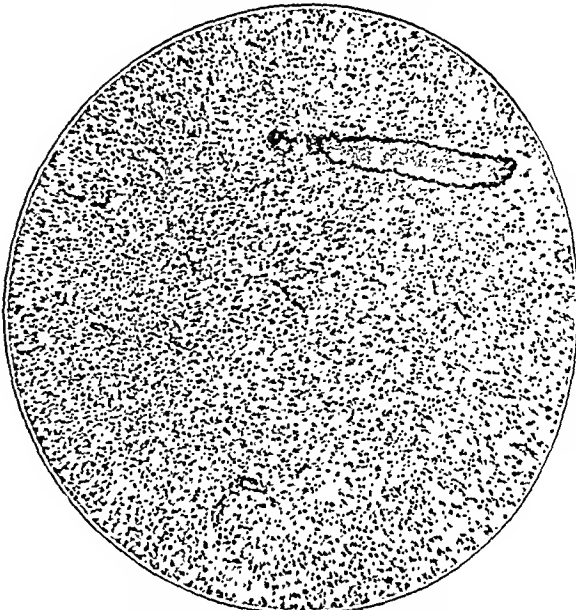


Fig. 3.—Section of monkey brain injected with emulsion of conjunctiva. Lower power magnification, hematoxylin and eosin stain.

filtrate were inoculated into three tissue cultures made up of embryonic guinea pig brain, fetal serum and buffered salt solution. A similar inoculum was put into cultures made up of embryonic guinea pig brain in buffered salt solution.⁹ Control cultures consisted of an identical preparation without inoculum. At the same time at which the cultures were inoculated, three mice were injected intracerebrally with 0.3 cc. of the unfiltered washings and three mice with 0.3 cc. of the filtrate. These animals, observed subsequently for six weeks, showed no symptoms.

Eight days after the cultures were inoculated the fluid portion was tested for sterility. At the same time 0.5 cc. was inoculated into fresh tissue cultures and 0.05 cc. was injected into each of six mice (intracerebrally). A portion of the fluid was also made up as antigen in the usual manner. Intradermal tests with this antigen gave positive results in four cases of venereal lymphogranuloma and negative results in two control cases. (B in the table). Fluid from the control cultures, on the other hand, gave no reactions (C in the table).

The results of the subcultures were negative, i. e. there was no indication of the presence of virus by mouse inoculation or by preparations of antigens from the cultures.¹⁰

Five days after inoculation two of the mice showed symptoms suggestive of a lymphogranulomatous infection: rough coat, humped back, emaciated appearance and ataxia. These animals were killed seven days after inoculation and from a 1:10 emulsion of the two brains antigen was made after part of the unheated emulsion had been passed to six mice. Of these, three showed the symptoms previously noted. This mouse brain antigen produced a positive cutaneous reaction in a known case of venereal lymphogranuloma (D in the table). We succeeded in transmitting the symptom-producing factor through passage in six mice.

9. A detailed account of the methods and preparations used here may be found in a recent study of the virus of lymphogranuloma in tissue cultures made by one of us (Sanders, Murray: J. Exper. Med. 1:113 [Jan.] 1940).

10. It is quite possible that the virus might have been transmitted serially in cultures if, instead of passing the fluid, an emulsion of the tissue and the fluid had been used as transfer inoculum. This fact was later established in other experiments with virus of lymphogranuloma in tissue cultures (M. S.).

A *Macacus rhesus* monkey was injected in the right parietal area with 1 cc. of an emulsion made by grinding up a small portion of excised conjunctiva of the patient with 2 cc. of Simm's solution. It is interesting to note that a portion of the same emulsion when used as an antigen gave positive reactions in cases of venereal lymphogranuloma and a negative reaction in a control case (E in the table).

Twenty days after inoculation a rise in temperature (to 103.4 F.) was noted, associated with transient weakness and tremors of the limbs contralateral to the site of injection.

On January 16, seven days after the onset of symptoms and twenty-seven days after inoculation, the animal was killed. Grossly, except for a moderate hyperemia, the brain showed little variation from the normal. Microscopic studies of various portions of the brain revealed a mild inflammatory reaction about the blood vessels with some degenerative changes (figs. 3 and 4) in the lower layers of the cortex on the right side. Microscopic examination of the spinal cord and of abdominal and thoracic viscera revealed no abnormal changes.

COMMENT

Repeated positive Frei reactions with reliable human antigen leave no doubt that the patient had at one time been infected with the virus of venereal lymphogranuloma. Moreover, the febrile response to the first intravenous injections of Frei antigen was typical of a patient infected with venereal lymphogranuloma (Hellerstroem,¹¹ Decker, Cañizares and Reider¹²). The serum protein values in this case were normal.

With regard to the site of inoculation, there was no history and no evidence (scars) that the virus had entered the body through the genitals. The anal fistula may have been non-specific, since in the later course nothing in the rectum (absence of stricture or ulceration) suggested lymphogranuloma of the rectum.

The conjunctivitis of the right eye, however, followed the typical course of an infection with the virus of venereal lymphogranuloma. The infection spread to the lymph vessels and the regional lymph nodes and was in later stages of the disease characterized by chronic edema. As in the case reported by Levaditi, Bollack, Basch and Desvignes,² there was no pain associated with the optic process.

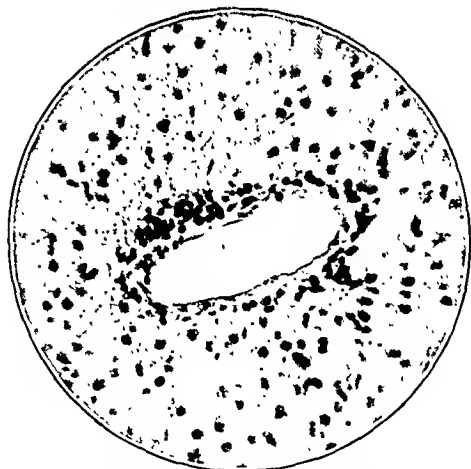


Fig. 4.—Section of monkey brain injected with emulsion of conjunctiva. High power magnification, hematoxylin and eosin stain.

Syphilis, tularemia and tuberculosis as etiologic factors of the ocular disease were ruled out. *Leptothrix* was not seen at biopsy.

Therapy with intravenous Frei antigen was not carried very far. Its failure is not surprising in view of the poor results in cases of late venereal lymphogranuloma of the genitals (esthiomene, ulcerations) in which stasis and edema are far advanced.

Sulfanilamide, however, terminated the activity of the process of the eye. Its efficacy in this case points to the infectious nature of the lesion. Besides, sulfanilamide, although to a lesser degree than sodium sulfanilate,¹³ seems to be valuable especially in the later stages of venereal lymphogranuloma.

It is interesting to note that by intradermal tests on patients the virus was demonstrated in an extract of the tissue but not in washings from the eye. The virus was demonstrated, however, in cultures made from these washings. It seems probable that this intracellular virus was present in the washings in quantities too small to produce a positive Frei reaction without preliminary enrichment in culture.

SUMMARY

A third case of chronic unilateral conjunctivitis of seven years' duration due to the virus of venereal lymphogranuloma was observed. Treatment with sulfanilamide was effective in stopping the active process and in reducing the accompanying edema and stasis. Vision of the eye, however, had already been destroyed several years before. Demonstration of the virus by tissue cultures suggests that this technique may be a more delicate means of demonstrating the presence of the virus than animal inoculation.

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CORONARY THROMBOSIS OCCURRING IN A PILOT WHILE IN FLIGHT IN A SINGLE SEAT AIRCRAFT

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The prevention of any medical incident sufficient to incapacitate an individual while in flight is the primary duty of every physician charged with the care of fliers.

Although this medical incident may occur in any form, such as grand or petit mal, fainting from any cause, decreased judgment, perception and reaction time from any other illness or anoxemia, it is unusual to diagnose the precipitating cause, owing to the finality of the resultant crash.

In prevention, unfortunately, the inability to prognosticate in most cases the individual who will develop such an incident as a coronary infarct is well recognized. This difficulty in the Army Air Corps is mainly overcome by limiting older pilots to flying duties of a less fatiguing nature than actual combat flying and by placing them in multiposed ships as command pilots with other pilots at the controls. Semiannual physical examinations, with electrocardiograms and teleroentgenograms once a year also aid in relieving from flying duties those individuals with obvious defects.

However, in addition to the older pilot, the rapidly growing literature of coronary occlusion, now being more frequently diagnosed in the third and fourth decades, must also direct our attention to the possibility of this lesion in the younger pilot. It is believed that the case described here demonstrates the advisability of electrocardiographic studies in the annual examination of pilots of all age groups, instead of limitation as now done to those over 45 years of age. These studies would not only indicate the rare occasion when some pathologic condition might be suggested for further investigation, but also accumulate data in a controlled group which would prove of inestimable value for study and correlation in later years.

This case of coronary occlusion occurring in flight, in a single seat pursuit ship (type P-36), is reported because of its unusual form and its occurrence in an apparently healthy man of 27 in whose case another crash, "cause undetermined," might have been added to that list already too full. One similar case of coronary occlusion while in flight in a 35 year old pilot was reported by Benson.¹

REPORT OF CASE

History.—The pilot, a second lieutenant, Air Corps Reserve, aged 27, had been on active duty with the Air Corps from March 30, 1939, to the date of his death, May 23, 1939. He had

11. Hellerstroem, J.: *Bull. soc. franç. de dermat. et syph.* 38:588 (April) 1931.

12. Decker, D. A.; Cañizares, Orlando, and Reider, R. F.: *Mouse Brain Antigen*, *Arch. Dermat. & Syph.* 40:397 (Sept.) 1939.

13. Hebb, Arthur; Sullivan, S. G., and Felton, L. D.: *Pub. Health Rep.* 54:1750 (Sept. 29) 1939.

1. Benson, Otis O.: *Coronary Artery Disease: Report of Fatal Cardiac Attack in a Pilot While Flying*, *J. Aviation Med.* 18:81 (June) 1937.

originally entered the Air Corps as a flying cadet July 1, 1932, and remained on active duty until Feb. 6, 1935. All previous physical examinations and the medical history obtained were essentially negative. From the period February 1935 to his entrance again on active duty in March 1939, I had examined this officer at six month intervals to fulfil the requirements of the semiannual examination of the Air Corps, with no abnormalities of the cardiovascular system being noted. No electrocardiograms were made. As a whole, he was considered one of the better physical specimens in a group of 200 highly selected and physically fit individuals.

On the day of his death, through history obtained from fellow officers, he awakened feeling perfectly well, ate a normal breakfast, and departed on a routine flying mission at 8:30 a. m. in a single seat pursuit ship. This mission did not necessitate altitudes in excess of 5,000 feet, but whether he may have flown to a higher altitude on his own initiative is not known. However, as he was a capable officer and obeyed orders, the latter event is not considered likely. On landing and climbing out of his ship at 9:30 he complained to a fellow officer that he was sick with epigastric distress and appeared cyanotic, weak and profusely perspiring. He was taken to his quarters in this fellow officer's car and walked to his room without aid at approximately 10 o'clock. No medical officer was informed of his condition until 12:30 p. m., at which time a visitor entering his quarters found him lying on his bunk, dead.

Additional history obtained after a search of his effects revealed that for approximately two months previous to his death, and from a time antedating his entry to active duty, he had been taking sulfanilamide prescribed by civilian physicians. This information had been withheld from the Army medical officers.

Autopsy.—This grossly demonstrated essentially the following: The weight of the heart was approximately 300 Gm., with a few petechial hemorrhages in the epicardium covering the posterior surface of the left ventricle. No valvular lesion was present. There was a slight amount of atherosclerosis in the arch of the aorta and considerable arteriosclerosis of the coronary system, with no gross evidence of roughening or superficial ulceration of any atheromatous plaque.

Other changes were found in congestion of the meninges and the brain with a slight amount of subarachnoid hemorrhage, congestion of the lungs, myocardium, spleen, liver, kidneys, pancreas, adrenals and genito-urinary tract, as well as a slight chronic adhesive pleuritis. The marked hemoconcentration was considered evidence of shock.

Microscopic Examination.—This was reported as follows: "Sections of the heart show ischemic infarction of the myocardium with round cell infiltration and the remains of some pigment. These foci without other evidence are quite suggestive of coronary artery disease. One of the forwarded sections shows a thrombus in a branch of coronary artery within the myocardium, although distinct ischemic changes are not present in the myocardium in this section. The thrombosis is recent and the material in some places is still adherent to the intima. The chronic passive congestion of the lungs is also in line with the left-sided cardiac changes. The small perivascular hemorrhages in the brain are generally regarded as secondary to anoxemia, usually terminal. It would seem that the cause of the sudden death is adequately explained by coronary occlusion by thrombosis."

COMMENT

The summation of evidence in this case points to arteriosclerosis of the coronary arteries with coronary occlusion by thrombosis, and probable insufficient time for gross alterations to become evident in the myocardium. As this cause was not definitely determined by the pathologist until after microscopic examination, any gross evidence of ulceration of an atheromatous plaque may have been so insignificant as to have been overlooked at the time of autopsy.

There appears to be no doubt that the terminal event took place in the air in the flight described. The possibility that the use of sulfanilamide was a contributing factor, with the formation of methemoglobin in the production of an anoxemia precipitating this event, is also present. Studies on the effect of anoxia on the cardiovascular system undertaken at the

School of Aviation Medicine, Randolph Field, Texas, have revealed significant changes in the electrocardiogram at altitudes as low as 5,000 feet in normal persons. The latter would also add credence to the theory of anoxemia while in flight as a causative factor in this case.

School of Aviation Medicine.

OCCUPATIONAL DERMATITIS FROM HANDLING RESIN-LINED TIN CANS

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In the course of the study of hazards to the skin in the canning industry of California we came across a number of cases of dermatitis diagnosed by the local physicians as "can poisoning." We were puzzled by the term, not knowing whether it meant that the workers were affected with dermatitis from the contents of the can or from some other substance with which they came in contact during the process of filling the cans. It never occurred to us that the condition might come from new, unused tin cans. However, while making studies in a number of canneries, we found that the workers engaged in

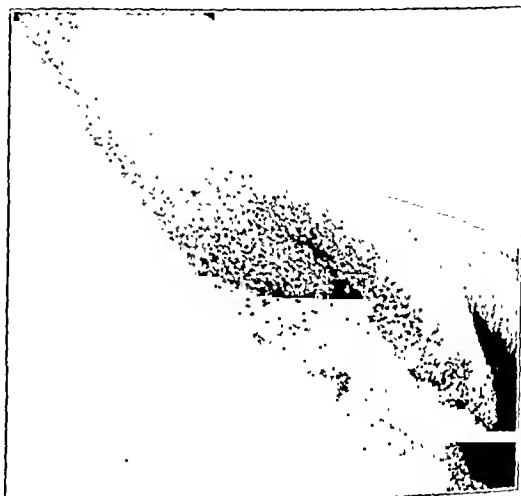


Fig. 1.—Dermatitis of axilla caused by dust from new resin-coated tin cans.

removing the new, unused tin cans from the freight cars and storing them in large storage rooms and then again removing them from the storage rooms to the traveling belts from which they are filled suffered from a dermatitis located principally in the cubital spaces and axillae. They claimed that this dermatitis was caused by dust coming out of the new cans, which at first seemed highly improbable, but actual investigations showed that such was the case. In the freight cars containing the cans and in the storage rooms in which they were stored there was a considerable quantity of metallic colored dust.

In one cannery three of the "forkers" were found to be affected (figs. 1 and 2). The forkers are the workers who move the tin cans from place to place by means of a contrivance called a fork, which consists of a handle across which at right angles there is a long piece of wood on which there are a number of forklike projections so spaced that each one fits into a can. By means of this a dozen or more cans can be lifted at one time. The three workers affected were patch tested with dust gathered from the traveling belt on which cans were placed. The dust was allowed to remain on the forearms for twenty-four hours and two of them showed a positive reaction.

Inquiries in other canneries elicited the fact that in some of them there had been cases of what they also called "can poisoning" at certain times among the forkers. It was found in other canneries examined that they had had no such cases.

Samples of the dust were obtained for chemical analysis from the cannery in which the three cases were seen. The dust was

found to consist principally of tin, iron and resin. The nature of the resin was that of a vinylite resin, but the exact composition of it could not be determined. Inquiry of the management of this cannery revealed the fact that about 10 per cent of the cans which they purchased were coated with a resin. Resin-lined cans were used for fruits and juices that might be discolored by contact with tin. Among such fruits are cherries and raspberries. Inquiries from a cannery where no such cases had occurred showed that they did not use any resin-lined cans.

Since the resin coating of cans is a comparatively recent process, and since no cases of dermatitis have been reported from tin or iron, it seems likely that this dermatitis was caused by sensitivity to the resin coating on the inside of the can, some of which flaked off in the form of dust.

An examination of the manufacturing process of these cans was made, but the actual composition of the resin coating was not disclosed by the manufacturer. The enamel or lacquer is applied to the clean tin plate as a thin film of the solution, after which the plate is passed through baking ovens wherein the volatile substances are completely evaporated from this film and the solid material polymerized or oxidized, thereby converting it into a hard, insoluble, highly chemical-resistant film of resin.

From the research department of the company manufacturing such cans the information was obtained that "the liquid enamel or lacquer which is applied to the tin plate is of a complex nature, consisting of a mixture of plasticizers and resins heavily bodied and reacted by heating. This is then thinned to the desired consistency and total solid content, for proper application, by means of a nontoxic petroleum solvent, similar in nature to that used in the varnish industry. Quite generally a lead-free drier is incorporated in the liquid enamel so as to facilitate the oxidation and polymerization of the film in the baking ovens. In general, the enamel is baked on the tin plate at a temperature of around 400 F. for a period of approximately 20 minutes. The finished enamel film weighs approximately 4/5 milligrams per square inch of tin plate. The finished film is different in all its physical and chemical characteristics from the liquid enamel film as applied to the tin plate."

In a personal interview with some of the chemists of a company manufacturing resin-lined cans it was learned that in addition to vinylite resin, which is used, there are certain plasticizers and driers the nature of which was not revealed.



Fig. 2.—Dermatitis of cubital space caused by dust from new resin-coated tin cans.

It was impossible to return to California and apply the different ingredients that go to make up vinylite resin lacquers to the skin of the three workers seen in the cannery. Therefore, it can be stated only that these workers were sensitive to the finished lacquer. The finished lacquer, however, may contain the polymerized resin, the plasticizer (which may consist of such chemicals as tung oil or China wood oil, or dibutylphthalate, or tricresyl phosphate), and a drier in the form of an inorganic salt of a resin, and fatty acids. Judging from our past experience, it is most likely that the sensitizer in the lacquer is one of the plasticizers. It may be possible, however, that in the baking process a decomposition of the resin takes place, because it is well known that vinylite resin, when coated over zinc, tin or iron surfaces and subjected to a temperature of 350 F. for a period of twenty minutes or more, shows a discoloration. Such a chemical reaction may result in the

formation of zinc chloride or tin chloride, both of which are known to be skin irritants. That it is a sensitization dermatitis is shown by the fact that these workers all give a history of having worked for a considerable time before they were affected. That it is caused by sensitivity to the lacquer in the dust is shown not only by the patch tests but by the history that when workers who were affected were removed from their work as forkers to another part of the plant the condition cleared up. Similar cases occurred only in canneries where lacquered cans were used, and such "can poisoning" has occurred only since resin-lined cans have been used.

We were unable to find the exact chemical causing the dermatitis because we could not obtain full cooperation from the companies making the cans as to the exact composition of the lacquer and because we were unable to get the affected workers for more patch testing, owing to the distant location of the factories and the seasonal type of the work.

We are reporting these cases because it is the first time that such cases have been reported and because we feel certain that it was the resin coating of the tin cans that caused the dermatitis.

FAMILIAL EOSINOPHILIA

REPORT OF A CASE WITH BIOPSY OF LIVER

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The term familial eosinophilia implies the presence of an increase in mature eosinophilic leukocytes in the blood of several members of a family in whom none of the known causes of eosinophilia, such as allergic states, dermatoses and parasitic infestations, are found. In 1911 Klinkert called attention to this condition and reported a family of six with eosinophil counts ranging from 7 to 15 per cent; three of the children, however, exhibited allergic manifestations. In 1930 Armand-Delille, Hurst and Sorapure¹ reported a family in which a boy of 8 had an eosinophil count of between 51 and 62 per cent with a leukocyte count that at times reached 29,000. Three sisters and one brother had eosinophil counts of 14, 27, 27 and 21 per cent, while the father had one of 7 per cent. Two other children had normal blood counts. In 1933 Sloan Stewart² reported four families in each of which several members exhibited a distinct, persisting and unexplained eosinophilia. There are many cases reported in which there are high eosinophil counts associated with a high leukocytosis, but in searching through the literature I could find only five families on record who showed a persistent unexplainable eosinophilia in several members of the family.

REPORT OF CASE

A Mexican woman aged 25, admitted to the charity clinic of Robert B. Green Hospital on Aug. 22, 1938, complained chiefly of sacral backache, which had begun soon after the birth of a child three months previously. The sacral backache was accompanied by a sense of pelvic heaviness and slight leukorrhea.

The patient was thin and somewhat anemic looking but did not appear acutely ill. The skin was smooth and normal in appearance. No areas of pigmentation were seen. There was no enlargement of the thyroid gland or lymph nodes. The head, neck, heart and lungs were essentially normal. Inspection of the abdomen revealed an umbilical hernia of moderate size. The blood pressure was 130 systolic and 90 diastolic, the pulse rate 80, the temperature 98 F. and the respiratory rate 24.

Pelvic examination showed an acquired retrodisplacement of the uterus and a third degree retroversion.

Laboratory examination gave the following results: There were 4,190,000 red blood cells, with a hemoglobin content of 80 per cent, and 27,100 white blood cells. The differential count revealed 16 per cent neutrophils, 24 per cent lymphocytes, 53 per cent eosinophils and 2 per cent basophils. Two days later the total white cell count was 30,000, with 70 per cent eosinophils. All the eosinophils were of the mature variety. The Wassermann and Kahn tests of the blood gave negative reactions. Urinalysis showed nothing abnormal. Repeated examinations of feces for intestinal parasites or ova gave negative

1. Armand-Delille, P. F.; Hurst, A. F., and Sorapure, V. E.: Familial Eosinophilia, *Guy's Hosp. Rep.* 80: 248 (April) 1936.

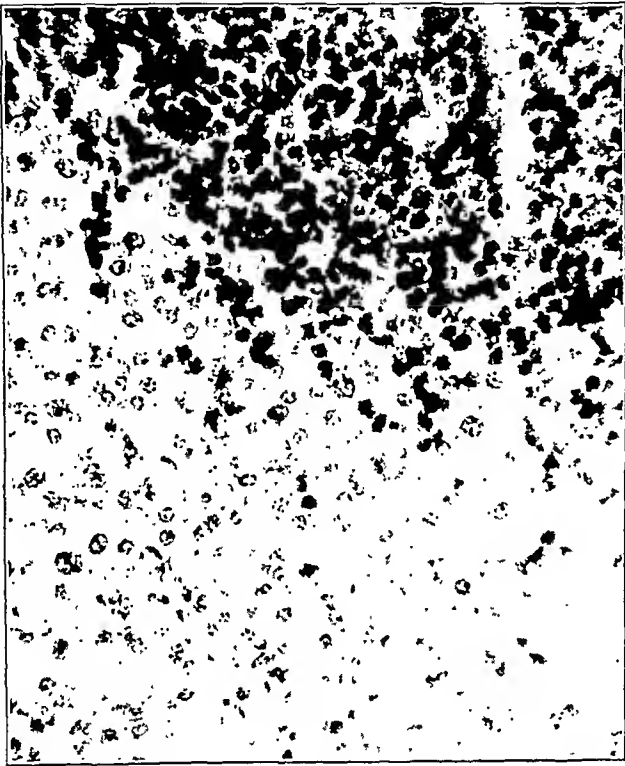
2. Stewart, S. G.: Familial Eosinophilia, *Am. J. M. Sc.* 185: 21 (Jan.) 1933.

results. An excess of neutral fats was found. The basal metabolic rate was plus 30. A study of the chemical changes of the blood gave the following results: nonprotein nitrogen 27.6 mg. per hundred cubic centimeters, creatinine 1.1 mg., sugar 79 mg. The icterus index was in units.

An x-ray study of the lungs showed considerable cloudiness and increased density in both lower lobes.

The patient was operated on seven days after her admission to the hospital. The operative procedure included laparotomy for the correction of the displaced uterus and repair of the umbilical hernia.

Inspection of the surface of the liver revealed numerous grayish white areas measuring from 0.5 to 1 cm. in diameter. The uninvolved intervening portions of the liver presented the usual appearance of the liver surface. One of the smaller areas, together with a bit of neighboring hepatic tissue, was excised



Dense infiltration of liver tissue with eosinophilic leukocytes, with complete replacement of hepatic cells in the center of the area.

for microscopic study. The sections showed dense infiltration of the liver tissue with eosinophilic leukocytes which resulted in complete replacement of hepatic cells in the center area, as shown in the illustration. Neighboring liver cells appeared normal.

Results of Subsequent Blood Examinations

Date	White Cells	Eosinophils, Per Cent
Sept. 3, 1938.....	10,800	24
September 7.....	19,700	53
September 11.....	16,450	58
October 4.....	42,700	81
December 15.....	20,100	59
June 28, 1939.....	10,650	34
Jan. 21, 1940.....	8,800	29

The postoperative period was uneventful. There has been a gain in weight of 20 pounds (9 Kg.) and the patient has enjoyed excellent health.

Subsequent examinations of the patient's blood gave the results tabulated.

The patient has two brothers and two sisters, all of whom, with the exception of one of the sisters, showed eosinophilia. A brother aged 11 years had a total white cell count of 7,550,

with 16 per cent of eosinophils, while the other brother, who is 8 years old, was found to have a total white cell count of 6,350, of which 15 per cent were eosinophils. The 5 year old sister had 6,000 leukocytes with a differential count showing 20 per cent eosinophils.

The patient's two children, a girl aged 4½ years and a boy aged 19 months, both showed an eosinophil count well above the normal limit, with total white cell counts of 12,400 and 10,300; the percentage of eosinophils was 31 and 13 respectively.

Blood examinations made on the patient's father, mother and husband showed nothing abnormal.

All members of the patient's family, and particularly those with eosinophilia, were carefully studied for evidence of the known causes of eosinophilia, with negative results.

COMMENT

This case is being reported because of the interesting gross and microscopic condition found in the liver, an addition, so far as could be determined, to previously reported cases of unexplained eosinophilia. It represents an unusual blood picture and presents difficulties in diagnosis, and the fact that the patient is one of four in a family of five children with eosinophilia and that her own children show a similar blood picture would seem to argue quite definitely in favor of a diagnosis of the familial type of eosinophilia rather than of eosinophilic leukemia as the explanation of the hematologic condition.

The elevated basal metabolic rate and infiltration of tissues with eosinophils are conditions recorded by Bass³ as occurring in eosinophilic leukemia. On the other hand, while it is true that in this case the eosinophils are of the mature variety, it is a noteworthy fact that there has not been a persistent increased white count.

205 Camden Street.

Therapeutics

THE THERAPY OF THE COOK COUNTY HOSPITAL

EDITED BY BERNARD FANTUS, M.D.
CHICAGO

NOTE.—In their elaboration, these articles were submitted to the members of the attending staff of the Cook County Hospital by the director of therapeutics, the late Dr. Bernard Fantus. The views expressed by various members are incorporated in the final draft for publication. When completed, the series will be published in book form.—Ed.

THE THERAPY OF SUBVITAMINOSIS B₁

IN COLLABORATION WITH DRS. EUGENE F. TRAUT AND
REGINA STOLZ GREENEBAUM

Subvitaminosis B₁, beriberi and thiamine deficiency are synonymous terms. "Dry beriberi," a peripheral neuropathy produced by vitamin B₁ deficiency, occurs in all economic classes in Chicago. It is especially common at Cook County Hospital because of the poverty of its patients. "Wet beriberi," characterized by peripheral neuropathy and edema, is much less common. It may be overlooked because in this form the peripheral neuropathy "is so often only mild or minimal."¹ Since the term "beriberi" is associated by many with "wet beriberi" of the Orient, the term "subvitaminosis B₁" seems preferable for the condition as we commonly see it.

3. Bass, M. H.: Eosinophilic Leukemia, Am. J. Dis. Child. 41: 1394 (June) 1931.

Dr. Fantus died April 14, 1940.

Dr. Norman Jolliffe, of New York, gave the authors important suggestions on this work.

Much of the information contained in this article was obtained from the series by the Council on Pharmacy and Chemistry and the Council on Foods, published in THE JOURNAL, Feb. 19, 1938, page 577, and subsequent issues, and from R. R. Williams and T. D. Spies "Vitamin B₁ and Its Use in Medicine," New York, Macmillan Company, 1938.

1. Jolliffe, Norman: Personal communication to the authors.

Crystalline vitamin B₁ hydrochloride has been named thiamin chloride or, preferably, "thiamine hydrochloride."

DIAGNOSIS

In the successful use of vitamins, as in all other therapy, correct diagnosis is essential. Vitamins are specifics for diseases produced by their lack. They are valueless, though usually harmless, unless a deficiency of them is present. Each vitamin is specific in the treatment of the symptoms resulting from a deficiency of it. It is not helpful in the amelioration of symptoms produced by a lack of other vitamins, although the conditions favoring an insufficiency of one frequently produce a lack of others.

CONDITIONS IN WHICH SUBVITAMINOSIS B₁ MUST BE SUSPECTED

Any patient may have a thiamine deficiency. The usual diet of refined foods deprives one of some of the richest sources of this vitamin and at the same time increases one's need for it. The body requirements for vitamin B₁ are thought to be proportional to the metabolic rate and the non-fat calorogenic (including alcohol) intake. A person who refrains from all food needs little vitamin B₁. A diet high in refined carbohydrates increases the need for thiamine. No food contains a large amount of vitamin B₁ comparable to the vitamin C content of orange juice. For example, an orange which furnishes 90 cc. of juice yields 45 mg. of ascorbic acid, nearly the daily human requirement. On the other hand, 3 ounces (90 Gm.) of liver or pork muscle or 1 ounce (30 Gm.) of shelled peanuts provides only from 16 to 25 per cent of the calculated thiamine needed daily by the average person. Much of what is contained in raw foods is destroyed by the heat of cooking or may be discarded in the water of boiling. The intake of vitamin B₁ of even the well-to-do probably allows little if any margin of safety. Any slight increase in need such as occurs with violent exercise or a mild infection may suffice to produce subvitaminosis B₁.

Thiamine deficiency must be suspected under the following circumstances:

1. Inadequate intake of foods containing vitamin B₁:
(a) In a charity hospital, poverty is perhaps the most frequent cause of an inadequate diet. The diet of the poor is likely to be rich in cheap refined sugars and starches almost devoid of thiamine but deficient in liver, eggs, whole grain cereals and nuts richer in thiamine but comparatively expensive.

(b) Ignorance of the essentials of an adequate diet is a very important cause of inadequate ingestion of vitamin B₁. Food faddists may suffer for this reason.

(c) Diets used in therapy, if continued for a long time, frequently contribute to this deficiency. Diabetic patients with their disturbed carbohydrate metabolism seem to need more of this substance. Poorly planned antiobesity diets are also likely to be deficient in vitamin B₁ as well as in the fat soluble vitamins A and D. It is worth observing that in spite of being low in absolute amounts of vitamin B₁ the vitamin calory ratio is usually better in well planned reducing diets than in prescribed high calory, vitamin-rich diets, and certainly the ratio is better than in the average American diet. Smooth diets for patients with colitis reduce uncooked food to a minimum, thus eliminating other important sources of vitamin B₁ such as whole grains.

(d) Chronic alcoholism is the most frequent predisposing factor in cases of severe involvement at the Cook County Hospital. Alcohol provides non-fat calo-

ries which increase the need for thiamine. "Alcoholic neuritis" has been definitely shown to be a manifestation of thiamine deficiency. Loss of appetite often follows a long spree. The chronic alcoholic addict with limited funds buys liquor rather than food. Absorption is impaired by the effects of alcohol on the gastrointestinal tract. In cases of "alcoholic cirrhosis" of the liver, utilization is also impaired. Thus the chronic alcoholic addict has increased need, diminished intake, faulty absorption and possibly impaired utilization.

(e) Absence of teeth, with resulting inability to chew foods containing thiamine, may be a predisposing factor.

(f) The intravenous administration of dextrose to a patient whose thiamine stores are depleted may precipitate clinical subvitaminosis B₁.

2. Inadequate absorption. (a) Persistent vomiting produced by esophageal or pyloric stenosis, hyperemesis gravidarum, chronic intestinal obstruction or any other cause may result in subvitaminosis B₁.

(b) Chronic diarrhea, regardless of etiology, interferes markedly with absorption. The cathartic habit may also prevent adequate absorption.

(c) Short circuiting of the bowel may deprive the patient of a large amount of absorptive surface.

(d) Achlorhydria and acylia are sometimes associated with vitamin B₁ deficiency. Whether this relation is accidental or etiologic is unknown.

3. Increased need. (a) Infection, especially if of long duration and associated with fever, predisposes to subvitaminosis B₁ by increasing the metabolic rate and diminishing appetite. Typhoid and tuberculosis are examples.

(b) Thyrotoxicosis is another predisposing factor.

(c) In pregnancy and lactation the needs of both the mother and the rapidly growing fetus or infant must be met. The pregnant or lactating woman probably needs about five times as much thiamine as a nonpregnant adult.

(d) Violent exercise increases the thiamine requirements by increasing the metabolic rate.

4. Disturbed utilization. (a) Liver disease in some way affects the ability of the body to store or utilize vitamin B₁ and therefore larger amounts of it must be supplied.

(b) Persons with diabetes mellitus seem to have an increased need for thiamine. Vitamin B₁ plays an essential part in intermediate carbohydrate metabolism, which is disturbed in this disease.

5. Disturbed distribution.

Arteriosclerosis interferes with the distribution of vitamin B₁ to the tissues. An intake adequate for young adults may be insufficient for the aged.

SYMPTOMS AND SIGNS OF EARLY SUBVITAMINOSIS B₁

The earliest symptoms of early subvitaminosis B₁ are usually those of a peripheral neuropathy. The pathologic change is degenerative rather than inflammatory; hence the condition is a neuropathy rather than a neuritis. The common complaints are paresthesias such as numbness, burning or tingling, lack of endurance in walking or cramps in the leg muscles. The nervous symptoms and manifestations are usually but not always first noticed in the lower extremities. They are frequently bilateral and symmetrical. The vibratory sense is diminished or lost. Ankle jerks may disappear. A difference in the intensity of the painful sensation produced by pricking the patient on a normal part of the

body contrasted with what he feels on an abnormal part is useful as a test in early subvitaminosis B₁.

Mild cardiovascular involvement shows itself as dyspnea on exertion, palpitation, fatigue and rapid pulse.

Diminished appetite with loss of weight may precede or accompany the other symptoms.

MODERATELY ADVANCED SUBVITAMINOSIS B₁

At any stage the patient may complain of pain along a nerve trunk, even along the intercostal nerves. The muscular weakness may lead to drop foot. Atrophy of the affected muscles develops. It involves the thigh with the progress of the disease. The knee jerks decrease or disappear. The upper extremities may then be affected in similar fashion beginning at the distal portions and extending toward the trunk. As the sensory changes advance, pain and numbness increase. The hypesthesia or anesthesia usually assumes a stocking or glove pattern.

Dyspnea is noticed on slight effort. The heart enlarges symmetrically or predominantly to the right or to the left. Peripheral vasodilatation may show itself as a pinkness of the hands and feet. When the blood pressure is taken the sounds over the brachial artery may be long and booming. The common electrocardiographic changes are inversion of the T wave in any lead and low amplitude and prolongation of the QRS. Diminution of bowel tone and of peristalsis results in constipation. Diarrhea may alternate with or replace constipation.

ADVANCED SUBVITAMINOSIS B₁

The muscular and sensory changes increase. They may involve the trunk. The patient then becomes bedridden. Contractures may develop. The only cranial nerves likely to be affected are the vagus and the abducens. Vagus involvement produces vocal cord paresis and possibly tachycardia. The oculomotor nerves, especially the abducens, may be affected in cases of Wernicke's syndrome, now recognized as a manifestation of subvitaminosis B₁.

As cardiovascular failure increases, breathlessness is accompanied by the accumulation of edema. Hypoproteinemia, frequently a concomitant effect of a diet low in vitamin B₁, contributes to the production of the edema. Subvitaminosis B₁ and hyperthyroidism produce the only types of heart failure marked by an increased velocity of the blood, resulting in a decreased circulation time.

Advanced emaciation may be masked by the increased retention of water in cases of wet beriberi.

NEUROPATHIES LESS GENERALLY ACCEPTED AS DUE TO SUBVITAMINOSIS B₁

"Diabetic neuritis" is now more generally recognized as resulting from thiamine deficiency. Postinfectious or toxic neuritis, trigeminal neuralgia, some cases of sciatica and herpes zoster may be manifestations of B₁ deficiency or may be complicated by it.

DIAGNOSIS

The diagnosis of subvitaminosis B₁ must be based on symptoms and physical signs until a satisfactory chemical method for determining thiamine absorption and utilization can be found for clinical use. The therapeutic test is at present less expensive than chemical determinations. Subvitaminosis B₁ must be differentiated from neuropathies of other origin. It is the one neuropathy in which treatment is dramatically successful. A therapeutic test is therefore indicated whenever lack of vitamin B₁ is the suspected etiologic factor.

While thiamine is the most commonly deficient vitamin, especially among the poor, its expense precludes its use as a placebo in a charity hospital.

TREATMENT

Prophylaxis.—An adequate diet is the best prophylaxis for subvitaminosis B₁. Each history should include a detailed account of the patient's food habits. Particularly in a charity hospital, the amount, kind and frequency of ingestion of meat, eggs, fruit, vegetables, nuts, bread and cereals should make up a paragraph of the history. The manner and duration of cooking vegetables with particular attention to the disposal of the water or juice should be noted. In spite of a good diet, peculiarities in individual metabolism may produce subvitaminosis B₁. Almost every one must be dietetically reeducated. The poor must be supplied with the wherewithal for an adequate diet. The daily requirement of vitamin B₁ varies. The average adult is believed to need from 1 to 1.5 mg., or from 300 to 450 international units, of thiamine hydrochloride daily, depending on his non-fat calorogenic intake. This is equivalent to from 10 to 15 international units per hundred calories consumed, assuming that the average diet affords 3,000 calories. The preschool child is thought to require at least 20 to 25 international units per hundred calories and the pregnant or lactating woman about 50 international units per hundred calories. In pregnancy or the puerperium a diet yielding 3,000 calories would require 5 mg., or 1,500 international units, of thiamine hydrochloride daily. With the heightened metabolism of thyrotoxicosis the patient should have from 1,500 to 3,000 international units, or from 5 to 10 mg., each day. To obtain an adequate amount of thiamine an adult should have daily at least 1 pint (500 cc.) of milk, one or two eggs, at least one serving of meat, two servings of fruit (one raw), two servings of vegetables (one a legume), nuts and whole grain bread and cereals. For a balanced diet butter should be added. Nuts are the richest of any of the ordinary foods in this vitamin. Peanuts and peanut butter are within the reach of even the poorest. Roasting and processing affect their thiamine content only slightly. Liver is desirable because of its high content of thiamine and many other necessary food elements. Pork muscle is much richer than other meats in vitamin B₁. Peas and other legumes, wheat germ and brewers' yeast are important sources of thiamine. Much thiamine is dissolved in water during the boiling of foods. People must be taught to use this water in soup. Prolonged cooking destroys vitamin B₁. In contrast to the other factors in the B complex known to be essential for human beings, thiamine is heat labile. Raw beans, for instance, are exceptionally rich in this substance; baked beans are almost devoid of it. Consequently rapid cooking in a minimum of water and utilization of that water are desirable.

Since it is difficult to obtain an adequate amount of this vitamin in unrestricted diets, therapeutic diets prescribed for long periods must be carefully scrutinized to prevent thiamine lack. The prevention of "diabetic neuritis" makes this consideration especially important in planning diabetic diets. Diets for gastrointestinal disease are likely to be deficient. Cutting down on roughage eliminates much thiamine-containing substance. This difficulty can be avoided by prescribing sufficient milk and eggs and by sufficiently restricting the use of refined carbohydrates. Diets low in protein tend to be low in vitamin B₁. They should not be continued over long periods.

In diets restricted in thiamine-containing foods, it is advisable to supply this vitamin in yeast, wheat germ, vitamin B concentrates or as pure thiamine hydrochloride. The supply of other vitamins and minerals must also be considered. The amount of vitamin B₁ found in many commercial polyvitamin preparations is insufficient, in the recommended dosage, to supply the body's need if they are the sole source of this vitamin.

The Therapeutic Test.—The response to an adequate dose of thiamine hydrochloride administered parenterally is usually prompt in alleviating the symptoms of vitamin B₁ deficiency. Thiamine hydrochloride will not affect symptoms of other origin. Vitamin B₁ is most effective when administered parenterally. The parenteral route is imperative in a therapeutic test to insure absorption. Thiamine hydrochloride is injected subcutaneously at Cook County Hospital because of its more gradual utilization by that route. Intravenous injection results in more rapid excretion and requires an intern's attention. The subcutaneous is as effective as the intramuscular or intravenous route. Although much larger doses have been recommended in the literature, we have found that a subcutaneous injection of 10 mg. daily is usually adequate; 30 mg. daily may be needed in cases of severe involvement. We recommend employing this dose for ten days in a therapeutic test. The first signs of improvement are disappearance of edema, slowing of the pulse (if it has been rapid) and diminution of neuritic pain, of paresthesias and of tenderness in the calves. An increased feeling of well-being is especially characteristic in the cases of mild involvement. Recovery of motion and sensory perception are much slower. They will not occur within the period of the therapeutic test. Reflexes usually return and atrophy disappears some time after the restoration of motor power. Alleviation of any of the characteristic symptoms and signs is a confirmation of the diagnosis of B₁ subvitaminosis.

If no improvement occurs after ten daily injections of 30 mg. of thiamine hydrochloride in the severe cases, and of 10 mg. in the majority of cases, curative effects are not to be expected. Another diagnosis should then be sought immediately. Thiamine treatment, itself innocuous, may be harmful by distracting the physician from a more thorough search for the true cause of the disability. We have seen a tumor of the spinal cord, syphilis of the central nervous system and nephrosis thus overlooked.

The Continuance of Treatment.—After the diagnosis of thiamine deficiency has been established by a favorable result of the therapeutic test, the underlying cause of the deficiency must be sought and, if possible, remedied. Injections of adequate amounts of thiamine hydrochloride must be continued until cure is effected. It is better to give too much than too little. This holds especially for cases of cardiac disorders, in which penurious dispensing may result in death. Giving thiamine hydrochloride in sufficiently large doses is economical in saving hospital days. Cook County Hospital saves by buying crystalline thiamine hydrochloride and making its own solution. Failure of absorption is avoided by the parenteral method of administration.

In the light of present information we recommend a daily injection of 10 mg. for the first few weeks, except in cases of very severe involvement, in which 30 mg. may be used for two weeks. More widespread use of acceptable excretion tests may alter this advice. The administration of the vitamin should continue until complete recovery has occurred. After the deficiency

is overcome, equilibrium should be maintained by an adequate supply in the food or by thiamine supplement if needed. The vitamin B₁ intake can be continued at the desired high level by supplying a diet containing wheat germ, yeast, rice polishings or their extract, liver, whole wheat bread and cereals, eggs, nuts, lean pork and legumes.

In addition to the parenteral administration of thiamine hydrochloride, a high intake of other necessary food elements is essential. When one vitamin deficiency exists, other food deficiencies are to be suspected. The components of the B complex are interrelated in the intracellular enzyme systems. With an adequate supply of all of them the patient will progress more rapidly than if some are missing. Since essential unknown dietary elements presumably exist, it is impossible to prevent all deficiencies with vitamin concentrates alone. Without clinical or laboratory evidence of a lack of other vitamins, it seems unnecessarily expensive to give other vitamin concentrates when the diet is adequate.

If a patient leaves the hospital before his cure is completed, the Visiting Nurses' Association of Chicago will continue his injections at home under a physician's supervision. Many hospital days may be saved by this service.

We caution against the intrathecal administration of thiamine. Convincing evidence that this is a safe method of administration is lacking. Its advantages over intravenous or subcutaneous injection have not been confirmed. Any of its reported good effects may be ascribed to the nonspecific benefit of an aseptic meningitis with the accompanying hyperemia of the meninges. We have had no experience with the massive doses prescribed by Naide² for the treatment of the ischemic pain in peripheral arterial disease.

The ultimate outcome of therapy and the rate of improvement depend on the duration and extent of damage. It is thought that the regeneration of nerves occurs at the rate of about 1 mm. a day. Months or even years may be required for complete regeneration of the nerves to the feet. In very severe cases of long duration with degeneration of the neurons in the anterior horns of the spinal cord or in the posterior ganglions, complete recovery may not occur.

ASSOCIATED CONDITIONS

Subvitaminosis B₁ and pellagra are frequently associated, especially in cases of chronic alcoholism. In such cases nicotinic acid should be administered in adequate doses in addition to thiamine hydrochloride. Riboflavin and vitamin B₆ deficiencies should also be sought, as should subclinical scurvy, subvitaminosis A and subvitaminosis D. In the presence of liver damage, subvitaminosis K may also occur. Achlorhydria and achylia are likewise frequent in cases of thiamine deficiency. Hyperchromic or hypochromic anemias are sometimes associated with a lack of the B vitamins. All these deficiencies should be appropriately treated if present.

Accessory therapy includes measures for the prevention of permanent deformities in paralyzed extremities. Moving all the joints passively through their full range of motion once a day prevents contractures. Holding the joints in one position in full casts encourages permanent stiffness and favors atrophy. Splints should be removable. Massage has been thought beneficial in improving the circulation of paralyzed muscles. Active exercise should be encouraged. Exercise should not

2. Naide, Meyer: The Use of Vitamin B₁ in Rest Pain of Ischemic Origin, *Am. J. M. Sc.* 197:766-773 (June) 1939.

be carried to the point of fatigue. We have seen no benefit from electrical stimulation.

Before discharge from the hospital the patient should understand the nature of his disease. He should be urged to continue to eat foods rich in thiamine and if necessary to continue the injections. Recurrences of thiamine deficiency are frequent.³ One should observe the patient periodically with this in mind. In cases of recurrences, it may be necessary to provide some sort of thiamine supplement indefinitely.

Special Article

CONFERENCES ON THERAPY

MANAGEMENT OF DIABETIC EMERGENCIES:

I. GENERAL TREATMENT

NOTE.—These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Management of Diabetic Emergencies: II. Treatment of Surgical Patients and Children."

DR. EUGENE F. DU BOIS: The management of the ordinary, uncomplicated case of diabetes is not difficult these days; the management of emergencies will always remain difficult. Dr. Tolstoi will take up the clinical aspects.

DR. EDWARD TOLSTOI: As the result of recent experiments performed in collaboration with Dr. Weber and Mr. Toscani, we have been led to adopt a somewhat less orthodox point of view in the treatment of the diabetic patient. We found that our experimental subjects were free from the symptoms of diabetes in spite of glycosuria when they were receiving a diet of 75 Gm. of protein, 60 Gm. of fat and 200 Gm. of carbohydrate, and protamine zinc insulin in daily doses of 50 units. Two rather unusual patients whom we observed in the metabolism ward for periods of fifty to sixty days maintained their weight. I want to emphasize this point. They also had no thirst or polyuria; they had no ketonuria, and they were in nitrogenous equilibrium in spite of the fact that they excreted as much as 150 Gm. of sugar some days, and in spite of the fact that there was an ever present postprandial hyperglycemia. From such experiments we postulated that for patients treated with protamine zinc insulin the guiding features of satisfactory treatment should be (1) the maintenance of weight, (2) freedom from symptoms and (3) absence of ketonuria. Furthermore, we were not concerned about the hyperglycemia or the amount of dextrose excreted. It is our belief that if the diabetic patient is made to utilize a quantity of carbohydrate essential for his particular metabolic needs the excess may be excreted without damaging results.

We have had further opportunity to pursue these studies in ambulatory cases in the outpatient department, and our results there have been gratifying. We paid little attention to the glycosuria; we were guided by the principles mentioned, and the majority of our patients have done exceedingly well. They have been liberated from multiple injections of insulin and now

receive one injection of insulin a day, putting their syringes away for the remainder of the time as they would their toothbrushes.

DR. DU BOIS: Are you referring to insulin now or to protamine zinc insulin?

DR. TOLSTOI: All reference will be to protamine zinc insulin unless I specifically state otherwise.

Simultaneously there have been others in the same field who have adopted the point of view that the patient may excrete sugar with safety. The quantity of sugar excreted in twenty-four hours has been a question of controversy. Some say a diabetic patient is well controlled when he excretes only 10 Gm. of sugar in twenty-four hours. Others permit him to excrete as much as 40 Gm. of sugar a day. Our patients excreted as much as 150 Gm. on occasions. Both of the patients whom we studied recently at this hospital excreted 100 Gm. daily for thirty days, a total of more than 6 pounds (3 Kg.) of sugar. They were in nitrogenous equilibrium and they felt perfectly well.

As to diabetic emergencies, there are in reality only two which are directly and intimately associated with diabetes. One of these is acid intoxication, or ketosis, and the other, which involves the insulin treated diabetic patient only, is the hypoglycemic syndrome.

ACID INTOXICATION

The chief causes for ketosis, the more hazardous complication of the two diabetic emergencies, are either medical or surgical infections—a common cold, a boil, a sore throat or the more serious conditions such as pneumonia or an acute surgical state of the abdomen. All of these are potential causes of ketosis. Others are departure from dietary restrictions and eating too much, the omission of insulin, and hyperthyroidism. This year I have had an opportunity of seeing two patients in whom stubborn ketosis developed during severe sunburn. It is noteworthy that a simple condition such as pharyngitis may decompensate the diabetic patient so that it precipitates not only ketosis but coma as well.

We should differentiate between the two terms "ketosis" and "coma." The clinical differentiation is especially important. Coma is a state in which the patient is unable to respond to any and all stimuli. In ketosis he may be up and about. The distinction between coma and ketosis has been made by a laboratory test by Joslin and his school. They feel that if the carbon dioxide combining power is below 20 the patient is apt to be in coma; if it is above 20 he is not in coma.

Let us consider how trouble arises for the diabetic patient who contracts an infection. First he takes less food because he loses his appetite. He has been taught that in such a situation he should omit his insulin. Here the fault lies with the physician who fails to realize that even though the diabetic patient does not ingest any food he will draw on his own storehouse. These foods cannot be utilized properly without insulin. The result is that ketone bodies begin to form. The little endogenous insulin that he may have is rendered less potent by the infectious process, which thus furnishes another factor conducive to ketosis. As the ketone bodies begin to form, the patient shows a characteristic syndrome that sets in rather insidiously. At first he feels weak and listless. He is perfectly content to be left alone. A little later thirst develops, and frequency as well as polyuria. He may also complain of headache, backache and aches in the calves of both legs. These symp-

3. Vorhaus, M. G.: Evaluation of Vitamin B (Thiamin Chloride) in the Treatment of Polyneuritis, *Am. J. M. Sc.* 198: 837-844 (Dec.) 1939.

toms are annoying, but they do not alarm the patient particularly until he begins to vomit. With the vomiting there is epigastric pain. This pain may further localize in the right lower quadrant. When the patient is seen at this time, the physician's attention is directed to the abdomen. An examination of the abdomen may show not only slight rigidity but even rebound tenderness. Appendicitis, of course, is the condition that suggests itself. At this point a blood count reveals leukocytosis with anywhere from 20,000 to 80,000 cells and a good percentage of immature neutrophils. Further examination of the patient will reveal that he is flushed; the tongue is parched, dry and beefy red, as is the throat; the eyeballs are soft; the skin is dry. The question arises: Is it uncomplicated ketosis or a surgical abdominal condition which has precipitated the ketosis?

Laboratory data at this point are of importance: in the blood sugar varying from 250 to 1,000 mg. per hundred cubic centimeters, low carbon dioxide combining power, elevated nonprotein nitrogen, hemoconcentration; in the urine large quantities of sugar, large quantities of acetone and diacetic acid. These establish the diagnosis. What are we going to do with a patient in this situation?

First, let us consider the one whose condition is not far advanced, the patient as we see him in the clinic. He may report a sore throat. Examination of the urine reveals a 4 plus acetone reaction and diacetic acid. The skin and the tongue are dry, there is dehydration and there are listlessness and the desire to be left alone. We tell the patient "Go home, take a tablet or two of table salt (1 Gm. of salt) every hour, and follow that with a glass of water; in addition, take all the hot salt broth you can." We teach him to examine his urine for acetone and tell him to do so every two hours, and as long as acetone is present to give himself insulin (regular soluble) after each urine examination until the acetone bodies disappear. The dosage of insulin is determined by the urine analyses for sugar. He is told to take 25 units if the result of the test is yellow or red, 15 units if the specimen is green, and the juice of an orange if the Benedict solution is unchanged after boiling. This simple rule also protects the patients against insulin overdosage. We have had such a patient come to see us on Friday and return on Monday weighing 8 pounds (3.6 Kg.) more and acetone free. Although the glycosuria was still present, she retained most of the fluid taken.

In the more advanced stages of ketosis the patient is admitted to the hospital and put to bed. Warm bags are applied to the extremities and he is wrapped in blankets. We cannot give this patient fluids by mouth because he is vomiting, so fluids are introduced by clysis. What kind of fluids? Dextrose solution, and since the patient is losing salt while losing water we give a saline solution of dextrose. It is well to start with 1,000 cc. of 5 per cent dextrose in saline solution. How much insulin? That varies; anywhere from 25 to 50 units. All agree that an amount above 50 units is unnecessary. Perhaps even smaller doses at frequent intervals are more effective than a single large dose. We have given 35 units at the start. The urine specimen is examined every hour or hour and a half for acetone bodies, and the administration of soluble insulin is continued until the ketone bodies vanish. As soon as the ketone bodies begin to disappear, the patient's flush vanishes, the tongue becomes moist, the cheeks fill out a bit and he is able to take some fluids by mouth. Salty broth is continued, also milk and orange juice are given, and

the urine is reexamined frequently. The administration of insulin is continued for a day or two after the ketone bodies have disappeared.

How much insulin should be given after the ketone bodies have disappeared? We use the simple guide just mentioned: If the urine specimen is yellow by the Benedict test we give 25 units; if it is green, 15 units. If it is blue we give only orange juice. After a two day period the patient will be able to take food by mouth, and he can then be regulated as any diabetic patient without ketosis.

As to the differential diagnosis of acute surgical conditions of the abdomen and ketosis, when a patient is admitted presenting the syndrome which I have outlined and we do not know the diagnosis exactly, my policy has been to postpone the operation if possible until the patient is ketone free. If he is ketone free and the abdominal symptoms persist, then I think he is entitled to an exploratory operation. There is one other test which I have found useful; namely, study of the leukocytes, not their number but rather the characteristic toxic granulation. I recall two instances of diabetic ketosis simulating surgical abdominal involvement without elevation of temperature or pulse rate, and with only 8,000 leukocytes in the peripheral circulation. The abdomen was tender with some rebound tenderness, and many granules were seen in the leukocytes. The acetonuria disappeared after insulin therapy, and as the patient appeared to improve surgical intervention was postponed. After two days of relative quiescence the temperature suddenly rose and an exploration revealed a gangrenous appendix. The other patient showed the classic picture of diabetic ketosis with dominant abdominal symptoms. The leukocyte count was not high, but toxic granules were present. In this case we did not wait too long. Insulin and an infusion were given and an acutely involved appendix was then removed at operation. The patient in whom ketosis is present without abdominal complications may show an even more marked leukocytosis, with a count up to 50,000 and more but, the absence of toxic granulation is conspicuous. I do not wish to convey the thought that the presence or absence of cells containing toxic granules is an infallible guide. It must be evaluated in relation to the other clinical and laboratory data.

HYPOGLYCEMIA

The other diabetic emergency is hypoglycemia. The syndrome which is caused by hypoglycemia is not the same with regular insulin as with protamine zinc insulin. The differentiation is very important. With regular insulin the patient has ample warning. He becomes nervous and apprehensive, begins to sweat, has headache, his memory becomes foggy, there are visual disturbances, and he realizes that something is wrong. Orange juice will correct the difficulty immediately. With protamine zinc insulin the onset of these symptoms is rather insidious. The only trouble may be headache; it may continue for six, eight or ten hours, and then the patient may go precipitously into hypoglycemic coma from which he cannot be aroused. We therefore tell patients who are receiving protamine zinc insulin "If and when you experience any unusual symptoms, no matter what they are, please take some orange juice at once and follow that up with milk and crackers." The reasons for that are probably obvious to all of you. The orange juice will counteract the existing hypoglycemia, while the milk and crackers, a cereal or bread will continue to supply carbohydrate to combat the prolonged action of the protamine zinc insulin.

The preparation of the surgical patient is a problem that all of you will encounter, and it is not difficult. With the emergency surgical condition such as acute appendicitis in diabetes, the patient is taken to the operating room. There he is given an intravenous clysis of 5 per cent dextrose in 1,000 cc. of saline solution, together with 25 units of insulin hypodermically. When he is returned from the operating room, the procedure is repeated. That will insure a flow of urine, which is frequently examined. The dose of insulin which is then given is determined by the rule I have already stated: 25 units if the reaction is yellow, 15 units if it is green, and only orange juice if the patient can take fluids by mouth and the reaction is blue. Continue with that until the patient is able to eat. Then give a simple diet and regulate it in the customary manner.

With the surgical condition in diabetes which is not an emergency, the procedure is slightly different. We all know that patients in the operating room lose a good deal of fluid, and I prefer to hydrate them for a longer period before operation. With those patients we advise the ingestion of table salt in a dose of 1 Gm. (two half gram tablets) every hour with a glass of water, for about ten or twelve hours before operation.

To recapitulate briefly: The most serious emergencies of the diabetic are (1) ketosis and (2) hypoglycemia. The treatment of ketosis is based on two definite scientific principles, the replacement of fluid and salts and the use of insulin. The treatment of hypoglycemia is based on a sound scientific principle as well, the administration of sugar. For the rapidly acting insulin sugar may be given in the form of orange juice and for the slowly acting protamine zinc insulin milk and crackers or some form of carbohydrate that is slowly absorbed so that it can neutralize the prolonged effect of the insulin.

There appears to be more to the mechanism and the treatment of diabetic coma than has been indicated in this discussion. There are factors about which a good deal still needs to be learned. We should not gain the impression that by the treatment outlined we are able to save all patients with diabetic coma. Under the most favorable conditions and the best treatment known, many of the patients still die, for reasons which in the present state of our knowledge remain unknown. This appears to be the general experience.

DISCUSSION OF QUESTIONS

DR. DU BOIS: Do you have much difficulty in getting a patient to take tablets containing salt (sodium chloride)?

DR. TOLSTOI: No.

DR. DU BOIS: How do you give them?

DR. TOLSTOI: Just let the patient swallow the tablet. If he cannot swallow the tablet, crush it and follow it with a drink of water.

DR. HARRY GOLD: One might give about one-sixth teaspoonful of ordinary table salt, could one not?

DR. TOLSTOI: Yes. We prefer the tablet form. It is convenient. However, salt in any form will do.

DR. McKEEN CATTELL: Your procedure is based entirely on the matter of replacing salt and fluid which is below normal?

DR. TOLSTOI: That is right. The diabetic patient in coma does not retain dextrose solutions alone for any length of time. The fluid is rapidly lost. The addition of salt helps to fix the fluid in the body. I am sure that some of the hospital staff will recall the patients who have come into the house as little shriveled up indi-

viduals and by the next day they seem like balloons, with big puffy cheeks and eyes that seem small, from edema resulting from the salt water treatment. Of course, as soon as the salt is discontinued the water flows off and the patient seems more normal.

DR. SAMUEL B. BARKER: Don't you think that the salt may have some effect in replacing the deficient base and in the differential excretion of chloride perhaps as ammonia chloride? That, of course, would not be a rapid process. Undoubtedly the main thing would be the salt itself, but don't you think the retention of base from the chloride would be an important effect of salt administration?

DR. TOLSTOI: That is quite true, because in these cases acetone is being produced all the time, and to neutralize that we draw on the body's supply of base. There are other points, too controversial, perhaps, to discuss here, namely the administration of sodium bicarbonate, gastric lavage and lactate-Ringer (Hartmann's) solution. I don't recommend them nor do I object to their use.

DR. DU BOIS: Of course, the question as to whether or not sodium bicarbonate should be used is at least thirty years old. The point about keeping the diabetic patient wet is also fairly old. I remember that at least twenty-five years ago Theodore Janeway used to insist on that: the wet diabetic patient did not go into coma.

DR. BARKER, will you continue the discussion of diabetic acidosis?

DR. BARKER: The term "acidosis" is rather unfortunate. It was introduced by Naunyn, who intended it to designate the production in diabetes of beta hydroxybutyric and acetoacetic acids, a situation which is now rather well covered by "ketosis." Acidosis has come to have such broad implications that it is often used to include practically all aspects of the condition resulting from the production of these two acids. The word itself is an exaggeration: the blood is seldom actually acid, in the sense that its p_H falls below 7.0, and often considerable amounts of ketone bodies are found in the blood without any deviation from the normal range of 7.3 to 7.5. Probably the best definition of the present day use of the term is that suggested by Van Slyke and Cullen: a lowered alkali reserve resulting from acid production. In the case of diabetes, acid production would be the production of beta hydroxybutyric and acetoacetic acids.

At the start of this short discussion on diabetic acidosis I should remind you that the fundamental cause of the extensive acid-base disturbances found in diabetes is the deficient carbohydrate oxidation. This leads to a deranged fat metabolism, with large amounts of the ketone bodies being produced from the incomplete oxidation of fatty acids. These are neutralized by means of base taken from $BHCO_3$, the carbon dioxide freed being eliminated by the lungs. The kidneys assist in the attempted regulation of normal equilibrium by excreting the acids partly in the form of free acid and partly in the form of ammonium salts. The kidney is able to form ammonia in order to conserve fixed base (that is, sodium). At this stage no change has yet been produced which is not rather easily reversible by remedying the primary cause, namely the poor oxidation of carbohydrate. The proper procedure is, of course, the administration of carbohydrate and insulin. This will stop the acid production and assist in the oxidation of any accumulated ketone bodies. The base combined with these acids is thereupon released and

serves to return the carbon dioxide combining power of the blood to normal.

However, if the diabetic condition is allowed to continue unabated, the organic acid load increases and the alkali reserve of the blood is still further reduced. Ammonia production by the kidneys is unable to keep up with acid excretion, and the use of fixed base is resorted to. This still further reduces the ability of the blood to carry carbon dioxide and at the same time lowers the total salt concentration. This hypotonicity is at once remedied by the excretion of water until the proper salt concentration is reached. This results in a temporary isotonicity but also produces a lowered total content of electrolyte and a lowered blood volume.

As the condition progresses still further, the amount of base available to carry carbon dioxide becomes small and the base from chloride seems to be freed to neutralize acid material. Hydrochloric acid often is vomited or may be excreted by the kidneys as ammonium chloride. The depletion of alkali and long continued glycosuria eventually lead to serious dehydration, hyperpyrexia and hyperpnea. In the extreme condition of diabetic coma, desiccation is pronounced, blood volume, alkali reserve and base content are very low, and the blood p_H may be below 7.1.

The changes as sketched here have been related to blood but of course apply to all extracellular body fluids. The cells also are hit by the loss of salt and water, but they are most affected by the self destruction induced by the increased breakdown of body protein. All the changes described are gradual; conditions merge into one another with no sharp demarcation. In addition to the tissue changes, there is pronounced dyspnea caused by the need of eliminating large amounts of carbon dioxide aggravated by hyperthermia and sometimes by increased metabolism.

The first line of treatment must still remain the alleviation of the defective carbohydrate oxidation with insulin, coupled with the administration of carbohydrate to replace the lowered body stores. Beyond that, one may look toward restoring the water and the electrolyte balances. The patient is dehydrated but, as Dr. Tolstoi has mentioned, the administration of water alone will not afford any permanent relief. The need for base is acute, but it is undoubtedly best to supply this as sodium chloride rather than as sodium bicarbonate, for two principal reasons: First, there is often a need for chloride as well as for base. If base is needed in larger amounts than chloride, the kidney is quite capable of excreting the excess of chloride as ammonium chloride, and the fixed base is retained. It is furthermore quite possible that the administration of sodium bicarbonate even in extreme diabetic acidosis may overcompensate and cause a dangerous alkalosis, when insulin is also used.

It may be reemphasized that the most logical treatment for the alleviation of diabetic acidosis is the use of insulin plus sugar, combined with salt administration.

STUDENT: I should like to ask Dr. Barker if he considers that the danger of acidosis is due primarily to dehydration.

DR. BARKER: Dehydration certainly is an exceedingly serious aspect of untreated acidosis. The diminished alkali reserve, lowered blood p_H , hyperglycemia and other carbohydrate disabilities, fatty infiltration and degeneration are all important involvements in diabetes and all are precursors of dehydration. But the dehydration and lowered blood volume are undoubtedly the factors which hit the hardest, in the final analysis.

The administration of base was an early treatment, but bicarbonate administration did not help permanently. Magnus Levy's old idea was that one should cause the patient to excrete as much acetone as possible; that it was more important to eliminate it than to keep it. Actually, an excretion of acetone bodies in the urine of a normal persons can be caused by giving a large amount of base.

DR. TOLSTOI: Isn't there a feeling among cardiologists that the reduction of blood volume is detrimental to the heart of the diabetic patient who has lost a lot of fluid and is one of the causes which finally is responsible for death?

DR. EPHRAIM SHORR: With respect to the cardiac accidents, we should remember that the proper function of the heart is dependent on a normal type of metabolism, a situation which does not exist in the absence of insulin. It seems to me that to regard cardiac failures and irregularities that occur as due to just one factor, such as the dehydration, is possibly a little unsafe. In working with hearts of diabetic dogs we have been struck with the rather profound changes which occur in the texture of the muscle. The diabetic heart becomes fragile and shreds easily. There are also some histologic deviations from the normal. Therefore I think more than just one factor is responsible for the failures which occur.

ROLE OF THE PITUITARY

DR. DU BOIS: I will ask Dr. Chambers to tell us something of his work on the role of the pituitary.

DR. WILLIAM H. CHAMBERS: There are several excellent reviews of this subject, by Houssay, in the May 1937 issue of the *American Journal of the Medical Sciences*, also by Long and Britton and by Riddle in the *Cold Spring Harbor Symposia* for the summer of 1937 and a review article by Russell in *Physiological Reviews* for January 1938. These reviews discuss the effects of the different endocrines on diabetes. Many different types of animals, from the toad to the dog, are used and it is difficult to put the data together and form any consistent picture.

The depancreatized dog is in a completely diabetic condition when insulin has been withheld for three or four days, or three or four days after the operation when the animal has been given no food. You are quite familiar with the picture: respiratory quotients of 0.70 to 0.73 in the basal condition and no rise in quotient with the introduction of dextrose. The D:N ratio is 2.8. This condition prevails for about two weeks of fasting, until the animal loses from 45 to 50 per cent of its body weight. At that time the creatine excretion rises very definitely in the depancreatized animal. Sometimes the nitrogen excreting increases. This is associated with a rise in the respiratory quotient to the protein level, indicating that the protein is handled as a normal animal would take care of it.

Barker has studied this condition in our laboratory and found that the rise in the protein metabolism is not an essential part of the picture. At this time the acetone bodies may disappear completely and the D:N ratio may fall to zero, meaning no dextrose excretion at all. When dextrose is given the respiratory quotient shows a rise, indicating that some of the dextrose can be oxidized. Here is a condition where the animal in the absence of insulin can oxidize some sugar.

Now, a similar situation is found, as you know, in the Houssay animal. Houssay in 1929 pointed out that the removal of the pituitary would change the diabetic

picture, lowering the D:N ratio, reducing the ketosis almost to zero and reducing the glycosuria. We studied several animals of this type in the calorimeter with the help of Dr. Chandler and Dr. Sweet and found that the respiratory quotients under basal conditions would range between 0.74 and 0.78. That is, the animals under basal conditions were burning some sugar at all times.

But when we gave them dextrose by mouth the injected sugar apparently was not burned. That is, there was little rise in the respiratory quotient, only five out of fifteen experiments showing any definite increase. About 60 per cent of the sugar was excreted. So we attempted a different type of experiment, one of which may serve as an illustration. The data are from one of nine dogs with which balance studies were made in the following fashion: The animal was given meat twice daily and put in the calorimeter for eight hours during the course of the day. The metabolism when the animal was quiet in the cage at night was probably quite equivalent to that in the calorimeter in the dark during the daytime.

We found that when the animal was on a pure meat diet for five days the D:N ratio was 2.46, that it excreted 40 Gm. of dextrose and the equivalent of 16 Gm. of nitrogen a day and that the respiratory quotient during the day averaged 0.75. This was not changed by the introduction of the meat. On the basis of a respiratory quotient of 0.75, in twenty-four hours the animal would oxidize about 30 Gm. of sugar.

In a subsequent period of three days we added to the meat, given twice daily, 30 Gm. of dextrose and some lard. The animal then excreted about 15 Gm. of the 30 Gm. which was fed over the amount which might be derived from the protein according to the D:N ratio. In other words, the animal was oxidizing 30 Gm. from the protein and 15 more from the extra dextrose, and 15 Gm. was recovered in the urine. The respiratory quotient rose to 0.78. Calculating from the heat production and the respiratory quotient, we find the dextrose oxidized in twenty-four hours to be about 50 Gm.

In a later experiment the animal was given 100 Gm. of dextrose a day for four days and 85 Gm. was excreted; the oxidation remained practically the same and the respiratory quotient about the same.

In other words, these animals lacking a pituitary and a pancreas are able to oxidize a limited amount of dextrose. An increased amount in the diet does not change the amount oxidized, but it is merely excreted.

You recall that Long has removed the adrenals from depancreatized cats and found that the diabetes was ameliorated in much the same way that Houssay showed with the hypophysectomized diabetic dogs. We have studied four adrenalectomized depancreatized dogs. The data from these animals could be put with the data from the Houssay animals and no distinction found. The D:N ratios and the respiratory quotients are about the same. The respiratory quotient shows no particular rise when dextrose is ingested. The removal of the adrenal seems to be quite comparable to the removal of the pituitary as far as carbohydrate oxidation is concerned.

In an article published in 1937, Long reported that adrenal cortex extract given in large amounts to rats which had been partially depancreatized produces a definite glycosuria. In the earlier reports, small amounts of cortical extract showed no influence on carbohydrate metabolism. We are not prepared to say

from our data to what extent cortical extract may influence carbohydrate metabolism. In one adrenalectomized depancreatized animal cortical extract was withheld for six days. There was no difference in the carbohydrate metabolism that we could determine.

Another animal was hypophysectomized and studied, and later the adrenals were removed and the same experiments performed. The results were quite comparable.

So the removal of the adrenals after taking out the pituitary apparently does not change the picture further. Long has suggested, I believe, that the pituitary acts through the adrenal cortex. I think that this still remains to be demonstrated.

Now I want to take just a minute to show quantitative relationships in these different animals. The first animal—and these are round figures taken from the experimental data, estimates rather than actual figures—is a normal animal fed with plenty of carbohydrate in the diet. When given 50 Gm. of dextrose, it will absorb about a gram per kilogram hourly in the course of four hours. Of that amount 40 per cent is oxidized and 60 per cent deposited as glycogen. Whenever dextrose is given we find that it is not immediately completely oxidized but is partly deposited as glycogen. The Houssay animal will oxidize about 10 per cent of the dextrose given. According to Houssay's figures about 20 per cent in this four hour period may be deposited as glycogen and the remainder, or about 70 per cent, excreted.

The completely depancreatized animal will oxidize none. Glycogen deposition has been shown to take place in the absence of insulin if the blood sugar is raised to an abnormally high level. But when the dextrose is given by mouth the blood sugar is not high enough to show a definite deposition of the glycogen and 100 per cent of the dextrose can be recovered in the urine.

We see on a quantitative basis that removal of the pituitary, and we might put the adrenal in the same category, does not by any means restore the animal to a normal position, either with respect to oxidation of dextrose or with respect to the deposition of glycogen.

There is one other complicating factor in the relationship of the pituitary and the adrenal. It is apparent from this picture that we did not obtain 100 per cent recovery from the diabetic condition by any means. In two animals we did find practically a complete restoration of ability to oxidize dextrose. One of these was a Houssay animal which showed in the histologic sections a very definite lesion in the region of the hypothalamus but a perfectly normal adrenal cortex so far as we could tell. The other animal was a depancreatized animal which never showed glycosuria. We could find no pancreas at autopsy. The animal burned sugar in normal fashion but the autopsy showed a cyst in the posterior lobe of the pituitary and marked atrophy of the adrenal cortex. So I think that the explanation of the parts played by the pituitary and the adrenal cortex is still decidedly theoretical.

DIABETIC TISSUE

DR. DU BOIS: We have heard about the diabetic patient and the diabetic dog. I wonder if Dr. Shorr will say a little about the diabetic tissue that has been studied.

DR. EPHRAIM SHORR: We have come to regard diabetes as a disturbance of the mechanism by which the various ductless glands regulate sugar metabolism, rather than a defect exclusively associated with an insulin deficiency.

It seems probable that tissues have a fundamental capacity to metabolize a wide variety of foodstuffs, including carbohydrates, which is essentially independent of the secretions of the ductless glands. This is evidenced by the observation that embryonic tissues are capable of sugar oxidation before the ductless glands appear. As organisms became more complex with evolution, the ductless glands developed and assumed control over this function, among others. This loss of independence was one of the penalties the tissues had to pay for their greater complexity and higher organization. It is amazing that, despite the millions of years of such servitude, an organism as well as isolated tissues can still give evidence of this primitive independence and burn sugar without the assistance of insulin.

Some experiments in our laboratory have a bearing on this point. You will recall that Dr. Chambers showed that animals with pancreas and pituitaries removed were capable of oxidizing more carbohydrate than animals with pancreatic diabetes. The improvement was, however, only partial. We studied the respiratory metabolism of tissues isolated from these animals and found that they were capable of an entirely normal sugar metabolism. It is apparent from these experiments in the Houssay animal that there must still exist other factors which inhibit sugar metabolism apart from the pituitary secretions. We then asked ourselves whether the superiority of isolated tissues over the whole animal might not reside in the degradation of these other inhibiting factors with time, when the tissues were removed from the body. This theory was then tested by the study of tissues from diabetic animals in the following manner: They were removed from the animals under sterile conditions. One portion of tissue was studied at once and found, as one might expect, to have no capacity to oxidize sugar. Another portion was incubated for ten hours at body temperature under proper conditions. At the end of ten hours, these tissues were found to have regained the normal capacity to oxidize carbohydrate. This occurred independently of insulin. Our working hypothesis is that during the period of incubation the inhibiting influences, whether pituitary or adrenal in origin, were used up. Now the tissues were free both of the sugar-accelerating hormone (insulin) and the inhibiting hormones and had resumed their innate capacity to oxidize this foodstuff without any hormonal help.

In view of what I have said, you may have been puzzled about the absence of any influence of this conception on the present treatment of diabetes, which you have just heard outlined. What you have heard has been a careful therapeutic regimen based largely on the conception of diabetes in the human being as a disease due to deficient insulin production. This does, indeed, represent a lag between the results of animal experimentation and their application to human disease. It is warranted, however, for the present, on several counts. The chief reason for this apparent disregard of polyglandular factors in human diabetes is that we know but little about the role of the factors, other than insulin. This difficulty in correlating animal experiments with human disease is also seen in exophthalmic goiter, in which, despite our considerable knowledge of the presence of thyrotropic pituitary factors which produce a comparable condition in animals, little or nothing is known of the way in which these pituitary factors act in the production of exophthalmic goiter.

We must also recognize that, while human disease is in many instances comparable to that produced in ani-

mals, there is a tendency for conditions in the human body to become more stable after an initial disturbance than in animals, where it is possible to influence the ductless glands in a much more profound manner. This stabilization of the human organism can also be seen in disturbances of sex physiology, in whose treatment various hormonal principles, particularly those of pituitary origin, have been much less successful than in animals.

Finally, there is some suggestion from the work of Young as to the way in which these two points of view, the polyglandular disorder as against the relatively stable metabolic disturbance dominated by one secretion, can be reconciled. Young has been able, by injection of pancreatic extracts into animals, to produce degenerative changes in the pancreas which are followed by diabetes. This diabetes differs in no way from the diabetes produced in animals by complete removal of the pancreas and is, once degeneration is extreme, a relatively stable condition. This state produced by pancreatic extracts might be the prototype of human diabetes.

The newer conception of diabetes, however, is so recent and so inadequately explored in the human being up to the present that we should not be discouraged about the fact that it is not reflected in our standard treatment of the disease. A few years may well bring about an entirely new picture as a result of insight gained into the possible mechanisms underlying this disease.

NATURE OF INSULIN

DR. DU BOIS: I would appreciate it if Dr. du Vigneaud would make a few comments on the present stage of development of the chemistry of insulin.

DR. VINCENT DU VIGNEAUD: Insulin is a protein. The molecule is made up of amino acids, and of such a number of amino acids that immediately the possibility of synthesis is out of the question at present. When you hear individuals talking about synthetic insulin you can rest assured that they have no concept of the subject, because that is out of the question at the present stage of development. Probably no subject in the field of biochemistry is at present being attacked more diligently than the chemistry of the proteins. It is particularly interesting to note that various laboratories of classic physical chemistry which just a few years ago would not think of working on a biologic substance are working on proteins from a physicochemical standpoint. This is indeed a significant development. Anything done on the chemistry of proteins will in turn throw light on the chemistry of insulin. Also anything done on the chemistry of insulin in turn has its significance to the chemistry of proteins.

The fact that insulin is a large protein molecule with molecular weight of about 35,000 leaves the hope of oral administration at the present time somewhat discouraging. It is true that insulin is destroyed by certain proteolytic enzymes, but that is not such a formidable barrier as the size of the molecule because there are various ways to get around the enzyme destruction. The real problem is the fact that the molecule is so large that it is difficult for appreciable amounts to pass through the membrane of the intestine. One approach is to attempt to dissociate this large molecule into smaller units and still retain activity.

An interesting chemical development has been the recognition by many that zinc must be present in order to obtain a form of crystalline insulin. The crystalline insulin is a zinc complex of this protein. Much work

has been done to find out whether other metals will serve. Of all the other metals that have been tried, cadmium, cobalt and nickel are the only ones that enable the insulin to be crystallized. The crystallization of insulin is now so successful that it is being done commercially and a solution of crystalline insulin is on the market. The relationship of these metals to the insulin and the nature of the linkage are attracting the attention of our group and many others.

Much work is still going forward on the composition of insulin. The entire insulin molecule is still not completely accounted for. Considerable work is also going forward on various physicochemical properties of this interesting protein.

STUDENT: Why is zinc used rather than any of the other metals you mentioned?

DR. DU VIGNEAUD: The fact that zinc was the first metal to be encountered in the work is perhaps one of the reasons. Furthermore, the pancreas contains a considerable amount of zinc and this likewise might have influenced the choice of zinc. The crystals we have so far made with cobalt are tinged a light pink and the nickel crystals have had a green tinge. The fact that the zinc crystals are colorless and the fact that zinc occurs in the pancreas are perhaps the main factors in favor of the choice of zinc.

DR. CATTELL: Is it known how the zinc acts to change the character of the molecule in relation to the matter of absorption?

DR. DU VIGNEAUD: Insulin free of zinc is physiologically active. If you assay one against the other carefully you do not find much difference in spite of the claims to the contrary. However, there is a real difference between protamine insulin and insulin. It is suspected that zinc aids in the combination of protamine and insulin. If there is any difference between zinc insulin and zinc free insulin, which as I say is questionable, I think it would rest on the possibility that zinc insulin has more of a chance of attaching itself to certain proteins at the site of injection and delaying absorption a little bit.

SUMMARY

DR. DU BOIS: Dr. Gold, will you close the conference with a brief summary of the ground covered?

DR. GOLD: In the conference today we have had an account of some of the fundamental background of diabetes. The concept of the mechanism of this disease has undergone revision. Some of the crucial experiments were related which signify that so-called pancreatic diabetes may really represent an endocrine imbalance in which several endocrine organs are involved, the pancreas, the pituitary and the adrenal. This is in line with the observation to which Dr. Shorr called our attention, that diabetic tissue possesses an innate capacity to oxidize foodstuffs without the intervention of hormones, and that the hormones serve chiefly to regulate this function.

How matters stand now in relation to the chemistry of insulin was considered by Dr. du Vigneaud. Insulin has not been synthesized. It is a protein, and its synthesis awaits further knowledge of the chemistry of proteins. Insulin has a very large molecule, a fact which probably provides a barrier to its absorption from the gastrointestinal tract. There is indication that zinc is essential for the crystallization of insulin. We have been told that enterprise in the field of insulin chemistry is extremely active.

A method for the clinical management of the diabetic patient was outlined in which freedom from symptoms,

the maintenance of body weight and the absence of acetone in the urine are regarded as the significant indexes of satisfactory control of the diabetic. Little attention is paid to the level of the blood sugar or the amount of sugar excreted in the urine. These patients are treated with a single daily dose of protamine zinc insulin sufficient to enable them to metabolize enough carbohydrate for their needs.

The treatment of the two important diabetic emergencies and their physiologic mechanisms were discussed, namely, coma due to ketosis and insulin shock. The conspicuous symptoms of ketosis were considered: the parched tongue and the dry and flushed skin, headaches, pain in the calves of the legs, and abdominal symptoms suggesting surgical abdomen. Emphasis was placed on the necessity for large quantities of fluid, salt and insulin in controlling diabetic ketosis. The symptoms of overdosage in the case of protamine zinc insulin are somewhat different from those in the case of the regular insulin, and more protracted treatment is necessary in the case of the former to insure against recurrence of the symptoms of shock because of the longer duration of action of the protamine zinc insulin.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

ANTIPNEUMOCOCCIC SERUMS

(See General Article, N. N. R., 1940, p. 429)

Antipneumococcic serum obtained from rabbits has been shown to possess less of certain disadvantages accompanying the use of serum obtained from horses. Rabbit serum furnishes antibodies of smaller molecular size, which are therefore expected to penetrate infected tissues more readily. A method has been devised to minimize reactions, an attribute of nearly all natural (raw) rabbit serum. Chills are reportedly somewhat more common with unconcentrated than with concentrated rabbit serum, but these have been modified by the oral administration of acetylsalicylic acid (0.9 Gm.) immediately before the serum is given. As with horse serum, all preliminary sensitivity tests for susceptibility to rabbit protein should be performed. The Council has recognized as acceptable only those antipneumococcic types of rabbit serum for which horse serum has been accepted for N. N. R. (I, II, IV, V, VII, VIII). With the exception of type IV, only these types of horse and rabbit serum are included in the U. S. Pharmacopeia. "The outside label must bear the name Antipneumococcic Serum and the specific type of pneumococcus represented, the genus of animal employed, when other than the genus *Equus*, the manufacturer's lot number of the serum, the name, address and license number of the manufacturer, and a statement of the date beyond which the Serum may not be expected to retain the potency prescribed by the governmental authority." U. S. P.

ANTIPNEUMOCOCCIC SERUM, TYPE I (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus *Lepus*, which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniae*) of one of the varieties known as type I . . ." U. S. P.

For standards see the U. S. Pharmacopeia XI, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose—Therapeutic, by parenteral injection, from 20,000 to 100,000 units." U. S. P.

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the age and condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneu-

mococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type I.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type I pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit as described by Felton (*J. Infect. Dis.* 37:199 [Sept.], 309 [Oct.] 1925; *J. A. M. A.* 94:1893 [June 14] 1930), the unit being one-hundredth cc. of the control serum distributed by the National Institute of Health. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type I pneumococcus antibody.

E. R. Squibb & Sons, New York.

Antipneumococcic Rabbit Serum, Type I, Concentrated.—Prepared from the blood of rabbits which have been immunized by repeated injections of type I pneumococci, according to the procedure suggested by Horsfall, Goodner, MacLeod and Harris (*J. A. M. A.* 108:1483 [May 11] 1937). After four to six weeks of immunization, the rabbits are bled from the heart, the fluid portion of the blood is separated from the corpuscles, and the antibody in the fluid is refined and concentrated by salting out with ammonium sulfate, the globulin fraction being retained. The final product contains merthiolate 1 in 10,000 and 0.2 per cent of phenol. The resulting solution is then tested in comparison with the standard antipneumococcic serum distributed by the National Institute of Health to determine the number of units of type I specific serum per cubic centimeter. It is then filtered through a Berkefeld filter and again tested for potency. After the results of the assay are known, it is filled under aseptic precautions into sterile vials, each containing at least 50,000 units. Marketed in packages of one vial containing 20,000 units and one vial containing 5 cc. of the same serum diluted (1:100) for the sensitivity test.

ANTIPNEUMOCOCCIC SERUM, TYPE II (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus *Lepus*, which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniae*) of one of the varieties known as . . . type II . . ." *U. S. P.*

For standards see the *U. S. Pharmacopeia XI*, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type II.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type II pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined, and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit as described by Felton (*J. Infect. Dis.* 37:199 [Sept.], 309 [Oct.] 1925; *J. A. M. A.* 94:1893 [June 14] 1930), the unit being one-one hundred and fiftieth cc. of the control serum distributed by the National Institute of Health. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type II pneumococcus antibody.

ANTIPNEUMOCOCCIC SERUM, TYPE V (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus *Lepus*, which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniae*) of one of the varieties known as . . . type V . . ." *U. S. P.*

For standards see the *U. S. Pharmacopeia XI*, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type V.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type V pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of

the unit, based on satisfactory protection tests in mice. The unit is one-five hundredth cc. of the control serum distributed by the National Institute of Health, for type V pneumococcus antibody. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type V pneumococcus antibody.

ANTIPNEUMOCOCCIC SERUM, TYPE VII (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus *Lepus*, which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniae*) of one of the varieties known as . . . type VII . . ." *U. S. P.*

For standards see the *U. S. Pharmacopeia XI*, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type VII.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type VII pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit, based on satisfactory protection tests in mice. The unit is one-nine hundredth cc. of the control serum distributed by the National Institute of Health, for type VII pneumococcus antibody. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type VII pneumococcus antibody.

ANTIPNEUMOCOCCIC SERUM, TYPE VIII (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus *Lepus*, which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniae*) of one of the varieties known as . . . type VIII . . ." *U. S. P.*

For standards see the *U. S. Pharmacopeia XI*, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type VIII.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type VIII pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit, based on satisfactory protection tests in mice. The unit is one-two hundred and fiftieth cc. of the control serum distributed by the National Institute of Health, for type VIII pneumococcus antibody. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type VIII pneumococcus antibody.

POLLEN EXTRACTS-CUTTER (See New and Non-official Remedies, 1940, p. 43).

The following additional forms of Pollen Extracts-Cutter have been accepted:

Acacia; Alder; Alfalfa; Alkali Rye Grass; Almond; Annual Blue Grass; Aspen; Barley; Bent Grass; Birch; Bract Scale; Bromine Grass; Broncho Grass; Canada Blue Grass; Clapproot Broom; Cheat Grass; Chrysanthemum; Clover; Coreopsis; Cosmos; Cultivated Rye; Curly Dock; Dahlia; Dandelion; Dale; Deodar Cedar; Elm; English Walnut; Eucalyptus; False Coastal Ragweed; Field Oats; Field Wheat; Goldcured; Grasswood; Hops; Incense Cedar; Kochler's Grass; Loenst; Mesquite; Mexican Tea; Monterey Cypress; Mountain Sagebrush; Mustard; Pasture Sagebrush; Pecan; Perennial Rye Grass; Pickleweed; Poverty Weed; Prairie Sagebrush; Privet; Quack Grass; Rabbit Brush; Rose; Salt Grass; Shasta Daisy; Sheep Sorrel; Slender Wheat; Southern Ragweed; Speargrass; Spiny Amaranth; Squirrel Tail; Sugar Beet; Sunflower; Sweet Vernal; Sycamore; Tall Oat Grass; White Valley Oak; Willow; Yellow Pine.

SILVER PICRATE-WYETH'S (See New and Non-official Remedies, 1940, p. 486).

The following dosage forms have been accepted:

Soluble Trituration Silver Picrate 20% with Boric Acid 80%: A soluble mixture of silver picrate-N. N. R. (20 per cent) and boric acid (80 per cent).

Silver Picrate Jelly, 0.5 Per Cent: A water miscible jelly containing silver picrate-N. N. R., 0.5 per cent in tragacanth jelly, 1.5 per cent.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, AUGUST 10, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick as proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

ELECTRICAL CONVULSION TREATMENT OF MENTAL DISORDERS

Since the convulsive treatment of schizophrenia was introduced by Meduna in 1934, many excellent results have been reported in the treatment of various psychoses with this technic. Moreover, the insulin-induced hypoglycemic shock described by Sakel has also had wide application. Now comes another variant of convulsive irritative therapy in the form of an electrically induced epileptic fit. In 1937 an Italian physician, Cerletti,¹ reported to the Psychologic Congress at Milan that an electric current passed through the head of a dog produced a typical epileptic fit. His collaborator, Bini, asserted that the brain of a dog had tolerated, without any apparent damage, a current of 3,000 milliamperes. The animal died when the duration of the passage of

the current was prolonged to sixty or ninety seconds. Bini believes that the duration of the passage of the current is more important from the point of view of any damage done to the tissue of the brain than the tension of the current. However, many physicians and physiologists who have had experience with such technics consider the assertion unbelievable and feel that under any circumstances the passing of electric current through the brain is a most hazardous procedure.

After much work on the technical details of their method, Cerletti and Bini¹ applied the method to patients with schizophrenia. They report that the electrically induced shock was characterized by an immediate and absolute loss of consciousness, which was followed in from two to four seconds by a convulsive fit. The patients are said to have slept longer than after metrazol shock and to have been of good spirits on awakening. The authors also report that the patients had no recollection of their experience and that the state of excitation frequently observed with metrazol therapy was absent. In some instances the shocks were repeated after several minutes. In a later report Fleming² describes the apparatus used and the technic of induction shock. The chief advantage claimed for electrical shock over metrazol shock is the instantaneous loss of consciousness and an absence of such surgical complications as dislocations, which occur with metrazol therapy. Some investigators,³ however, fail to see much difference in the incidence of complications with the two methods, and Bingel and Meggendorfer⁴ particularly report dislocations of the jaw and the shoulder joint and fracture of the humerus and the scapula. Various investigations both in this country and abroad indicate that at least 1,000 persons have already been subjected to this technic.

In the meantime the possibility of serious danger associated with such a technic should not be overlooked. The passing of electric current through the body is always a matter for careful consideration. If the heart is included within the field, low tension currents are dangerous. True, if a current is passed from one to the other side of the head the percentage of current passing through the heart is much less than if the current is passing from arm to leg. In many studies which have been made on the effect of electric current on the brain it has been shown that, when the source of the current is a spark coil at 140 cycles per second with a peak voltage at the break of 220 volts and a resistance of the animal body of 1,640 ohms, a duration varying from three to fifty seconds may result in capillary hemorrhages, ganglion cell changes of swelling and

2. Fleming, G. W.; Golla, F. L., and Walter, W. G.: Electric Convulsion Therapy of Schizophrenia, *Lancet* 2:1353 (Dec. 30) 1939.

3. Sogliani, Giorgio: Eine neue Methode der Krampftherapie: die Elektroschocktherapie, *Deutsche Ztschr. f. Nervenhe.* 149:159 (Nos. 3 and 4) 1939. Braunmühl, A.: Der Elektrokrampf in der Psychiatrie, München. med. Wchnschr. 87: 511 (May 10) 1940. Bingel and Meggendorfer.⁴

4. Bingel, A., and Meggendorfer, F.: Ueber die ersten deutschen Versuche einer Elektrokrampfbehandlung der Geisteskrankheiten, *Psychiat. neurol. Wchnschr.* 42: 41 (Feb.) 1940.

1. Cerletti, U., and Bini, L.: *Boll. Acad. med. rom.* 64: 36, 1938.

shrinkage satellitosis, gliosis and demyelination. Morphologic changes in the brain may of course occur with both insulin and metrazol shock therapy. Sufficient data are apparently not yet available to determine whether irreversible changes are produced in patients after several shocks.

It should be obvious from what has been said that electrical shock to the human body may produce fundamental changes in the tissues which are sufficient to threaten life itself. Certainly before extensive clinical application is made of the passage of electric current through the brain, careful histopathologic studies of the brain under varying conditions should be attempted. Finally, the Council on Physical Therapy may well give careful study to the various devices employed in this technic with a view to checking the adequacy of safeguards over the current and voltage and technic of application involved in this procedure.

SICKNESS ABSENTEEISM IN INDUSTRY

The fundamental objective of industrial hygiene is to reduce loss of time, absenteeism and short work spans in industry. In a recent report before the Air Hygiene Foundation, Lanza and Vane¹ called attention to the importance medically and economically of industrial absenteeism in this country. Employers have on the whole been indifferent about lost time from sickness or injury not associated with work as a cause, since disability of this type is not compensable under the law and the costs are difficult to assay. However, evidence from a variety of sources indicates that losses in wages and through disruptions in production schedules must be estimated in billions of dollars each year. Records of sickness benefit associations provide the best available statistical information on lost time in industry. Even these records are frequently of limited value either as an index of incidence or for purposes of comparison. Bookkeeping methods in different industries and occasionally in different units of the same industry are based on totally different conceptions of recording absences. Furthermore, disabilities lasting less than one week are seldom reported since they are not eligible for benefits. Other variables involve sex, age, income and home surroundings of workers, all of which may have greater importance in the production of disability than the nature of the work.

The most reliable available data indicate that the average worker in the United States loses something over nine days annually to disabling sickness. As a rule there will be more sickness among women employees than among men both as to frequency and as to duration and more among married than among single women. Of this total about one day of absence is caused by industrial accidents and occupational diseases. The remainder of the lost time is due to diseases and com-

plaints not directly associated with work as a cause and which make up the bulk of general practice everywhere. These proportions appear to be roughly correct whether the absences are of longer or of shorter duration. True, many of the short term absences are chargeable to personal reasons rather than to sickness. Lanza and Vane support the observation that sickness-prone individuals exist. Although they constitute a small percentage of total employees, they account for an inordinately large number of lost days from illness. So far it has not been possible to associate sick proneness and accident proneness, although it is suggested that some correlation may exist. Rigid standards of preemployment physical examination are not the solution, since even in such physically picked groups as the military services noticeable degrees of absenteeism are encountered.

Lanza concludes that industrial sick absenteeism can be reduced by intelligent coordination of effort between employer, worker and the medical profession. Much reliance must be placed on the private physician, since so many of the causes of lost time fall directly in the province of private practice. Plans are now being formulated designed to provide means for the uniform reporting and recording of all absences in industry no matter what the cause or the duration. Progress in reducing sick absenteeism will take a large step forward as these procedures are generally adopted. The medical profession can make a considerable contribution to knowledge of disease frequency and severity both in industry and in the general population by cooperating in these developments.

Current Comment

BIRTHDAY VOLUME FOR FRANK HOWARD LAHEY

The many friends, both lay and medical, of Frank Howard Lahey have just published a birthday volume¹ in his honor. It is dedicated with the following statement:

All men desire to be immortal but few fulfil that desire in life. Yet fame gives immortality; and to have attained immortality in sixty short years is an enviable achievement.

We of the medical profession, partakers of that fame which you have gained for us no less than for yourself, offer to you this birthday volume, in which you will find yourself reflected more often than we intend to confess. You have honored medicine, and medicine delights to honor you. This is our birthday gift to you, our friend, adviser, and inspiration.

Yet we alone could not have made this offering. You have been a friend to many. It is fitting, therefore, that some of those to whom you have been physician, healer, and friend, should have made possible the publication of this volume. With it, they also offer homage to one of whom it may be said:

I am a man who has many friends . . .
And many friends have me.

The book contains principally scientific discussions dealing with surgery. There is, however, one exceptional essay on group medicine and the Lahey Clinic

1. Sick Absenteeism in Industry, Bull. 4, Medical Series, Air Hygiene Foundation, Inc., Pittsburgh.

1. Frank Howard Lahey Birthday Volume. Springfield, Ill., Charles C. Thomas, 1940.

which points out that there is no standardized form of group practice, that private groups are as diversified as hospitals, medical schools or universities, and that the Lahey group is one which has become particularly distinguished for its contribution to medical education and medical investigation. The volume is in its appearance and in its contents distinctive among publications of this type. It honors a physician whom all of us have just honored by his election to the Presidency of the American Medical Association.

COMMITTEE ON HEALTH RESORTS GATHERS INFORMATION

Pursuant to the action of the House of Delegates, the Board of Trustees of the American Medical Association appointed a committee of five to be known as the American Medical Association Committee on American Health Resorts.¹ The purpose of this committee is to collect and compile information on so-called health resorts, which are defined by the committee as follows:

An institution or region which gives major attention to the use of the special climatic and other natural therapeutic resources, including mineral waters, peloids (moor baths), etc., with which it is endowed by reason of its location. While the use of the natural resources is the prime object or purpose of the institution, other remedies may be applied as an adjunct.

The information collected by a questionnaire devised by the committee, and now in the mail, will be assembled temporarily in the committee's office in the Bureau of Health Education. A list of institutions to receive questionnaires has been compiled from records available in the headquarters office of the Association and from other sources. Such a list is not complete. The committee therefore desires to request that physicians, and the superintendents of institutions of the type described in the definition, communicate the names of such institutions to the Committee on American Health Resorts, American Medical Association, 535 North Dearborn Street, Chicago. Questionnaires will be mailed on receipt of names of institutions. The primary purpose of the committee at present is to assemble information on all institutions of the nature described.

YOUTH LOOKS AT CANCER

The Westchester Cancer Committee, Bronxville, N. Y., has prepared a book¹ designed to inform boys and girls of high school age about cancer. The little book, attractively printed and illustrated, can be read easily in thirty minutes and it provides in brief, condensed form all the essential information about cancer. The Westchester Cancer Committee believes that the high school student "faces the problem without fear and

consequently, if informed at this most receptive time of his life, will handle with intelligence a cancer problem coming into his later life. He will also take home correct information to parents, many of whom are unable to read English." This attack on the cancer problem is in line with the feeling of many persons experienced in health education who believe that the so-called adult type of health education, as distinguished from formal instruction in elementary schools, is most effective when concentrated on students of high school age. At this age young minds are fresh and, despite their pose of boredom with education, they are keen to learn what really interests them. Cancer, although curable in its early local stage, continues to increase. The educational movement for the control of cancer is still young as modern public health movements go. It will require at least another decade to make an appreciable impression on the mass of ignorance, prejudice, superstition and fear which surrounds cancer in the public mind.

INFANT AND MATERNAL MORTALITY AMONG NEGROES

In each of eight states there are more than 10,000 Negro births annually. As in other aspects of public health, the separation of figures on infant mortality among Negroes from the often considerably different conditions among the white populations of the same areas is of fundamental importance in evaluating actual conditions and needs existing. Tandy,¹ in a recently released statistical study of infant and maternal deaths of Negroes in the United States, points out that more than half (55 per cent) of the Negro births are attended by nonmedical persons—generally untrained or poorly trained midwives. Indeed in seven states, roughly those with the largest Negro populations, midwives attend more than two thirds of the Negro births. Of the 21,000 Negro infants who die each year in the United States, 11,000 die in the first month of life. Natal and prenatal causes are responsible for 41 per cent of the deaths, respiratory diseases for 19 per cent, gastrointestinal conditions for 11 per cent, all other diseases for 13 per cent and unknown and ill defined conditions for 16 per cent. Probably adequate antepartum and postpartum care would materially reduce this infant mortality. This condition is, moreover, paralleled by the maternal mortality rate for Negroes—a rate during the period of 1936 to 1938 of more than double that for white women. This is also susceptible of improvement through better antepartum and intrapartum care. The instruction and supervision of midwives have already begun to show some effect on the trend of infant and maternal mortality among Negroes. The improvement already manifest can doubtless be further extended; the development of consultation services, for example, should be of practical value. This study furnishes a much more satisfactory basis for constructive work in medical care than less critical statistical reports which fail to differentiate between particular groups of the population and their specific health needs.

1. The members of the committee are Dr. Bernard M. Fantus, professor of therapeutics, University of Illinois College of Medicine, Chairman (deceased); Dr. Walter S. McClellan, medical director Research Division, Saratoga Springs Commission, Saratoga Springs, N. Y.; Dr. William P. Holbrook, 4 East Congress Street, Tucson, Ariz.; Dr. Miletus B. Jarman, medical director the Homestead, Hot Springs, Va.; Dr. Euclid M. Smith, Medical Arts Building, Hot Springs National Park, Ark.

1. Youth Looks at Cancer, by the Westchester Cancer Committee, New York: Brookville Press, Inc., Brookville, N. Y., 1940, price 75 cents.

1. Tandy, Elizabeth C.: The Health Situation of Negro Mothers and Babies in the United States, U. S. Department of Labor, Children's Bureau, Washington, D. C., July 1, 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

COMMITTEE ON MEDICAL PREPAREDNESS

Report of Meeting Held at American Medical Association Headquarters, July 19, 1940

The following were present:

Dr. Irvin Abell,	Dr. Fred W. Rankin,
Chairman,	Dr. Harvey B. Stone,
Dr. Charles A. Dukes,	Dr. Samuel E. Thompson,
Dr. Roy W. Fouts,	Dr. Arthur W. Booth,
Dr. Stanley H. Osborn,	Dr. Nathan B. Van Etten,
Dr. John H. O'Shea,	Dr. Olin West,
Dr. James E. Paullin,	Dr. Morris Fishbein
Dr. Walter G. Phippen,	

and, by invitation, Dr. Thomas Parran, Surgeon General of the Public Health Service; Colonel Love, United States Army Medical Corps; Colonel Gibson, United States Army Medical Corps; Captain Sutton, United States Navy Medical Corps; Dr. R. G. Leland, Bureau of Medical Economics; Dr. William D. Cutter, Council on Medical Education and Hospitals, and Dr. C. M. Peterson, Council on Industrial Health.

In opening the session Drs. West, Abell and Fishbein discussed the necessity for coordination of various activities such as those of the governmental services, National Research Council, Advisory Committee on National Defense and the American Red Cross in order to avoid a considerable amount of confusion, which is already apparent.

THE QUESTIONNAIRE

Dr. West reported the work of the Committee up to the time of the meeting, including the development of the questionnaire, and reported that 165,000 questionnaires had already been distributed. It is evident that much editing and checking will be required in the handling of the questionnaires. There will also be the necessity for a considerable amount of follow-up in order to secure complete returns.

NEED FOR COORDINATION

Attention was called to the fact that many organizations of physicians had offered their services through the Committee, including the American Heart Association, the National Organization of Women Physicians, the National Medical Association and similar bodies. Apparently some of these associations had been specifically asked by various governmental agencies to undertake certain projects. It was voted that a message be drafted and sent to the Advisory Committee on National Defense and to the President, calling attention to the fact that the Committee on Medical Preparedness meeting with representatives of governmental agencies already finds evidence of duplication of effort and of much confusion and that it is felt that the early appointment of a coordinator for medical and health services is greatly desired in order to speed mobilization of medical resources for any emergency.

Dr. West then reported to the Committee the names of the physicians selected as chairmen for the various states. These were approved as published in THE JOURNAL for August 3.

INFORMATION ON MEDICAL PREPAREDNESS

Plans were developed for extending information developed through the Committee on Medical Preparedness to the medical profession through the use of the editors of the various state journals and the executive secretaries of the various state medical associations. It was pointed out that in several states committees on medical preparedness have already been developed and are functioning. In some states return postal cards have been sent to each member of the state medical association urging immediate return of the questionnaire and asking the member to return the postal card indicating that he has responded.

Other problems discussed at the morning session concerned a request from the British embassy for American physicians who wish to serve in Great Britain, the problems of aviation medicine, the use of refugee physicians and the support of medical education.

VACANCIES IN MILITARY MEDICAL SERVICE

Representatives of the Army and Navy Medical Corps pointed out that there are already vacancies both in the regular corps and in the reserves. The Navy particularly requires younger men in the lower grades in the reserves—especially in the capacity of junior and senior lieutenant.

The problems of industrial medical service were discussed, especially the need for training men for such positions.

An extended discussion was also held on the organization of the reserve corps and on physicians who would be available through membership in these reserve corps. Representatives of the Army, Navy and United States Public Health Service reported the work carried on to the present, involving relationships with other organizations such as the American Psychiatric Association, the American Public Health Association and similar groups.

NEED FOR PHYSICIANS TO CONDUCT EXAMINATIONS

There was indication of the need of physicians in relationship to physical examinations of young men in vocational training, WPA workers and those associated with the National Youth Administration.

TRAINING OF INDUSTRIAL PHYSICIANS

It was proposed that a resolution be developed requesting funds to permit the United States Public Health Service to aid in the training of industrial physicians and to cooperate with various schools of industrial medicine for this purpose.

Also discussed was the question of the use of part-time consultants by various services.

EXEMPTION OF STUDENTS, INTERNS
AND RESIDENTS

A resolution was prepared and sent to the Advisory Committee on National Defense and to the President, to Congress and to various governmental agencies regarding the desirability of maintaining medical education, internships and hospital residencies throughout any emergency.

FUNCTIONS OF THE COMMITTEE

After extended discussion of the organization within the individual states and counties, a subcommittee was appointed to prepare an outline of the functions of the members of the National Committee on Medical Preparedness and of the chairmen of the state committees. This was published in *THE JOURNAL* last week.

THE EXECUTIVE COMMITTEE

In view of the death of Dr. Austin A. Hayden, who was a member of the Executive Committee of the Committee on Medical Preparedness of the American Medical Association, Dr. Irvin Abell was elected to the Executive Committee to replace him. The other members are Drs. Olin West and Morris Fishbein.

ESSENTIAL TEACHERS

In order to aid the continuation of medical teaching, it was decided to request the executive committee of each of the medical schools of the United States to send to the Committee on Medical Preparedness a list of the personnel essential for teaching the student body of the size now existing.

EDUCATION THROUGH MEDICAL SOCIETIES

Plans were also made for each medical society throughout the nation to develop contact with representatives of the Army and Navy Medical Departments and the United States Public Health Service, with a view to arranging programs of education for civilian practitioners regarding the fundamentals of enrolment in such services.

It was urged also that members of the Committee on Medical Preparedness be available to medical organizations for addresses regarding functions of the Committee.

A procedure was adopted for calling the Committee on Medical Preparedness into special session and also for a meeting in the headquarters office of the American Medical Association of the state chairmen.

PLANS FOR CONSCRIPTION

Information was developed indicating that the setting up of a plan of conscription would involve a number of local draft boards in the individual states, with the sending of the men for examination to perhaps 100 different localities established throughout the United States for final military examination. In each of these hundred localities approximately eleven physicians would be required—men qualified in the medical specialties—to make final examinations so that individuals unfit for service would not be sent to camp, the idea being to have the examination as near as possible to his home and thus to disrupt his economic relationships as little as possible. Attention was called particularly to the need of specialized service for the examination of x-ray films of the chest for the detection of tuberculosis.

ENROLMENT OF VOLUNTARY
BLOOD DONORS

The American Red Cross, acting at the request of the Surgeon General of the United States Army, has announced plans for the promotion of a nationwide corps of volunteer blood donors which would become part of the national defense program, when and if needed.

For the past four years twelve Red Cross chapters have been furnishing whole blood from volunteers to hospitals for civilian use. The new program will be patterned along similar lines, using plasma instead of whole blood.

A preliminary study involving 1,300 Red Cross volunteers in four cities throughout the country will be conducted under the direction of a special committee appointed by the National Research Council, including Dr. Cyrus E. Sturgis of the University of Michigan, Dr. Everett Plass of the University of Iowa, Dr. Alfred Blalock of Vanderbilt University and Dr. Max Strumia of Bryn Mawr Hospital, Philadelphia.

Dr. William DeKleine, medical director of the Red Cross, has said that the proposed plan for collecting blood is patterned after the blood bank idea except that plasma will be used instead of whole blood. Preliminary studies will be made to perfect methods of collecting, storing and administering plasma under conditions comparable to war-time emergency. Blood for this initial study will be furnished by volunteers at the various hospitals where members of the Research Committee are regularly employed. The plasma collected will be stored and used as emergencies arise at these hospitals.

After these preliminary investigations have been completed, the Red Cross will then work out with the medical department of the army plans for enrolling prospective donors in cities throughout the country where collecting centers will be established. Blood so collected will be pooled in large sterile containers, to simplify storage, in sufficient quantities to meet the emergency needs for treating the wounded.

Recruiting donors will be conducted by a special chapter blood transfusion committee which will include leading local physicians. The technical phases of the project will be performed by the medical staff of the cooperating hospitals. They will examine the prospective volunteers and make the necessary blood tests as well as doing the actual transfusions.

Plague in the United States.—From the time of the first appearance of plague in the United States in 1900 to Jan. 1, 1940, there have been recorded 499 cases with 314 deaths. These figures may not agree with those presented elsewhere, as they have been compiled from various sources; and it may be reasonable to assume that, because of conditions existing in the Chinese quarter of San Francisco during the first plague epidemic in that city, and other difficulties which hampered the work of investigation and control, a complete record of cases in Chinese was not secured. Human cases of the disease in the United States have been reported in eight states, in chronological order of first appearance as follows: California, 1900; Washington, 1907; Louisiana, 1914; Florida, 1920; Texas, 1920; Oregon, 1934; Utah, 1936; Nevada, 1937. The last human case of plague in the United States, up to Jan. 1, 1940, was reported in Millard County, Utah, on Dec. 4, 1939.—Hampton, Brock C.: *Plague in the United States*, *Pub. Health Rep.* 55:1143 (June 28) 1940.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Seven Cases of Poliomyelitis.—Seven cases of poliomyelitis were reported in Houston County, near Webb, July 17, according to newspaper accounts.

Changes in Health Officers.—Dr. Otis F. Gay, Ashland, head of the health unit in Clay County, has been appointed to a similar position in Butler County, succeeding Dr. William M. Askew Jr., Greenville, who resigned to enter private practice. Dr. David B. Snelling, Butler, health officer of Choctaw County, has been appointed in charge of the unit in Greene County, with headquarters in Eutaw. Dr. W. D. Burkhalter, Montgomery, will be acting health officer in Choctaw County until a permanent appointment has been made. Dr. Rutherford O. Ingham, Montgomery, has been appointed health officer of Henry County, with headquarters in Abbeville.

CALIFORNIA

Changes in Faculty.—The University of California Medical School, San Francisco, announces that the title "dean emeritus" has been given to Dr. Langley Porter. Dr. Porter retired this year. In 1936 he first retired from the deanship, to which he had been appointed in 1927, but following the death of Dr. Williams McKim Marriott, who died shortly after taking over the position, Dr. Porter again assumed the office. He has been associated with the school since 1918. His successor has not yet been named. Appointments announced at the school recently include Drs. Douglas G. Campbell as assistant clinical professor of psychiatry and Hubert R. Hathaway as assistant professor of anesthesia.

Courses for Practicing Physicians.—Postgraduate courses for practicing physicians will be conducted by Stanford University School of Medicine in cooperation with the San Francisco Department of Public Health and the San Francisco Hospital, San Francisco, September 9-13. Registration will close August 31. The fee will be \$25. The courses will cover pediatrics, gastro-enterology, surgical anatomy and operative technic, management of hypertension and nephritis, x-ray diagnosis and therapy, proctology, surgical emergencies, traumatic injuries and fractures, otorhinolaryngology and anesthesiology. In addition, general meetings will be held in the evenings with the following speakers: Drs. Windsor C. Cutting, Lowell A. Rantz and Arthur P. Richardson on "Chemical Warfare Against Bacterial Disease"; George S. Johnson, "Emotions at War" and Arthur L. Bloomfield, William Dock and David D. Mason, who will conduct a clinicopathologic conference. All fees are payable to the school of medicine; checks and applications should be mailed to the dean, 2398 Sacramento Street, San Francisco, not later than August 31.

Psittacosis Traced to Los Angeles Birds.—The California state department of health has traced a fatal case of psittacosis in Caldwell, Idaho, and three cases in Tucson, Ariz., to a Los Angeles pet shop, according to *Public Health Reports*, June 7. The Idaho case occurred in December 1939 in a person who had bought a pair of parakeets in November from a local dealer. The parakeets had been purchased early in November from the Los Angeles shop, and psittacosis was subsequently proved in all the birds in that lot as well as in other birds in the Los Angeles stock. No infection was found in the California aviaries that supplied the Los Angeles dealer, but as he had imported birds from other countries it seemed probable that the infection was introduced by the imported birds, according to the report. The Arizona cases occurred in a family which owned birds purchased in the same Los Angeles shop. When psittacosis was suggested the birds were set free and were therefore not available for examination. The patients were two young adults in the same family and a nurse who cared for them.

DELAWARE

Executive Secretary of Board.—Dr. Edwin Cameron, Morgantown, W. Va., director of the Monongalia County Health Department, has been appointed executive secretary of the Delaware State Board of Health, according to the *American Journal of Public Health*. The appointment was effective July 1. Dr. Cameron graduated at Dalhousie University Faculty of Medicine, Halifax, N. S., in 1927.

FLORIDA

Changes in Health Officers.—Dr. Leland H. Dame, West Palm Beach, has been appointed director of the Hamilton County health unit.—Dr. Irving E. Simmons, Quincy, has resigned as health officer of Gadsden County to become head of the new unit in Nassau County. Dr. Samuel J. Ravitch, Peekskill, N. Y., is acting director in Gadsden County.

Sectional Meeting on Surgery.—The Florida section of the Southeastern Surgical Congress will hold its seventh annual clinical conference at the Jackson Memorial Hospital, Dade City, August 31. Included on the program will be:

Dr. Robert L. Sanders, Memphis, Tenn., Complications of Peptic Ulcer.
Dr. William G. Hamm, Atlanta, Ga., Skin Grafting.
Dr. Thomas C. Davison, Atlanta, Breast Tumors.
Dr. Herbert Acuff, Knoxville, Tenn., Surgical Phases of Lung Abscess.
Dr. Edward Jells, Jacksonville, Carcinoma of the Stomach.
Dr. Louie M. Limbaugh, Jacksonville, Medical Care of the "Surgical" Diabetic.
Dr. Benjamin T. Beasley, Atlanta, Uterine Displacements with Demonstration of an Original Apparatus Designed to Treat These Conditions.

GEORGIA

Gift for Library.—A grant of \$10,000 has been allowed by the Rockefeller Foundation to purchase books and journals for the library of the University of Georgia School of Medicine, Augusta, according to the state medical journal. The grant will supplement the Moore Fund, given to the school by Mrs. Julia Carter Moore, Augusta.

Rabies Among Foxes.—The state department of health reports in its July bulletin an outbreak of rabies among foxes in three counties. During the past month, it stated, the heads of five foxes were received for examination. Two were too badly decomposed for examination, but three showed positive evidence of rabies. Foxes have also been found dead in one county without having external signs of the cause of death. A number of foxes attacking human beings and domestic stock have been reported. The counties involved are Burke, Jefferson and Jenkins. In March a hunting dog went rabid and while in the early stages bit several foxes, which escaped. About a month later a rabid fox was killed in the vicinity and several mules bitten by foxes later developed rabies. The reports on foxes attacking human beings, domestic stock and hunting dogs have been coming in constantly since that time. A plan is under way to investigate the outbreak under the cooperation of the Burke County board of health, the state department of health, the state wild life department, the federal biologic survey and the Rabies Research Laboratory of the Rockefeller Foundation.

INDIANA

Personal.—Dr. Aaron M. Winklepleck, assistant to the superintendent of the Indiana State Sanatorium at Rockville, has been appointed head of the Smith-Esteb Memorial Hospital, Richmond. He succeeds Dr. Robert A. Staff, who was recently named superintendent of the Indiana State Sanatorium.—Dr. and Mrs. Byron W. Marshall, Gary, were guests of honor at a farewell dinner recently given by neighbors, patients and friends on the occasion of Dr. Marshall's retirement from active practice and the couple's departure from Gary. Dr. George W. Gannon presented Dr. Marshall with an oil painting of a scene in Brown County, of which Dr. Marshall is a native and where he and Mrs. Marshall plan to live.

District Meeting.—The Eighth District Medical Society met in Elwood, June 19, and presented the following program:

Dr. Guy A. Owsley, Hartford City, Borderline Allergy in General Practice.
Dr. Bruce W. Stocking, Muncie, X-Ray Diagnosis in Abdominal Diseases.
Dr. George C. Stevens, Indianapolis, Mental Hygiene Clinic and the Physician.
Dr. Edwin Rogers Smith, Indianapolis, Use of Metrazol in Certain Mental Diseases.
Dr. John C. Drake, Anderson, Recent Advances in Treatment of Fractures of the Hip.
Dr. Willis D. Gatch, Indianapolis, Cause and Treatment of the Symptoms of Peritonitis.

Albert Stump, Indianapolis, counsel for the Indiana State Medical Association, addressed the dinner session on "Legal Problems in Care of Indigents."

IOWA

Health Exhibit at State Fair.—The Iowa State Department of Health will conduct an exhibit at the state fair, August 21-30, featuring the public health nurse and her work in connection with infant and child health.

Society News.—Dr. Harold Dabney Kerr, Iowa City, discussed "The Present Status of Radiotherapy" before a combined meeting of the Bremer County Medical Society and the

staff of Mercy Hospital in Waverly recently.—Dr. John H. Matheson, Des Moines, addressed the Hardin County Medical Society in Iowa Falls, June 25, on common diseases of the eye.—At a meeting of the Jackson County Medical Society in Bellevue, June 27, Drs. Horace M. Korn and Willis M. Fowler, Iowa City, spoke on "Diagnosis and Treatment of Cardiac Arrhythmias" and "Modern Treatment of Anemias."

KANSAS

Personal.—The staff of St. Margaret's Hospital, Kansas City, gave a dinner recently in honor of Drs. Richard C. Lowman, Kansas City, and Owen W. Krueger, Kansas City, Mo., celebrating their completion of fifty years in the practice of medicine. Dr. George M. Gray, Kansas City, treasurer of the state medical society, was also a guest and Dr. John F. Hassig, Kansas City, was the toastmaster.—Dr. Thomas L. Foster has been appointed superintendent of the Osawatimie State Hospital, effective June 1; he has been assistant superintendent of the Larned State Hospital for the past eight years.

MICHIGAN

Tuberculosis in Michigan.—Tuberculosis deaths for the whole state in 1939 held close to the record low of 1938, but rates of individual counties varied widely, according to a release from the state department of health. Deaths from tuberculosis in the state totaled 1,881 in 1939, showing a rate of 36.9 deaths per hundred thousand of population as compared with 1,866 deaths and a rate of 36.6 in 1938. Detroit had 945 of the 1,881 deaths in 1939. Crawford and Oscoda counties were free from tuberculosis deaths for the second consecutive year, and a third county reporting no deaths was Gladwin.

Changes in Health Officers.—Dr. Frank J. Hill, Waterbury, Conn., was recently named health officer of the Mason-Manistee health unit.—Dr. Clifton F. Hall, Big Rapids, has been appointed director of the Mecosta-Osceola health department; he has been acting director since October 1939.—Dr. Roelof Lanting, who, during a leave of absence as director of the Delta County health department, Escanaba, has been studying in the graduate school of public health and hygiene, University of Michigan, Ann Arbor, has been appointed director of health district number 7 with headquarters in Gladwin. Dr. Fred O. Tonney, formerly of Chicago, acting director of the Delta County unit, will remain there until a new director has been named before accepting a recent appointment to the staff of the state department of health at Lansing, newspapers reported.—Dr. Jacques P. Gray, Berkeley, Calif., has been appointed director of the Hillsdale County health department. In this capacity he will be a representative of the W. K. Kellogg Foundation in Hillsdale County, a unit of the Michigan Community Health Project.—Dr. Erwin F. Hoffman, Iron Mountain, has resigned as health officer of Dickinson County to join the Florida state department of health, Jacksonville.

MINNESOTA

Supreme Court Upholds Suspension of License.—The Supreme Court of Minnesota, May 17, in a unanimous opinion affirmed a ruling of the district court of Ramsey County that the order of the Minnesota State Board of Medical Examiners suspending the license of Dr. Gottfried Schmidt, Lake City, for five years "was neither arbitrary, oppressive nor unreasonable." The license was suspended by the state board, Dec. 16, 1938, following a complaint made by a former patient to the board. According to a report from the state board, the hearing brought out that Dr. Schmidt attempted to diagnose cancer, brain tumor, stomach ulcer and other serious ailments by having the patient moisten a piece of wood pulp paper with saliva and then placing the paper on the abdomen of the patient or on the abdomen of a woman employed by Dr. Schmidt in his office in Lake City. He also claimed that he had a machine with which he could broadcast treatments to absent patients. Dr. Schmidt was twice warned by the state medical board to desist from such practices. Justice Stone's opinion described Dr. Schmidt's diagnostic methods as "so clearly bald quackery, and so much an imposition on his patients, that the testimony of three patients with whom he had good luck would not have helped him." Dr. Schmidt was born in Minnesota in 1871 and graduated at the University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, in 1903. He had practiced in Lake City for twenty years, it was stated.

NEW YORK

Society News.—Dr. L. Whittington Gorham, Albany, addressed the semiannual meeting of the Montgomery County Medical Society, June 18, at Fort Plain, on "Differential Diagnosis of Coronary Occlusion."—Dr. Richard Nauen, Ray Brook, discussed diagnosis of tuberculosis at the semiannual meeting of the Medical Society of the County of Essex, June 4.—Drs. Ray D. Champlin, Oneonta, and John C. McClintock, Albany, addressed the Otsego County Medical Society, Oneonta, June 19, on "The Doctor in War Time" and "Preventing Complications of Thyroid Gland Disease" respectively.—At the semiannual meeting of the Steuben County Medical Society at the Veterans Administration Facility in Bath, June 13, the speakers were Drs. Heyward H. Hopkins, Rochester, on "The Vallium Cup"; Sidney N. Eichenholtz and Abraham Falk of the facility staff on "Low Back Pains" and "Undulant Fever" respectively.

New York City

Bequests to Hospitals.—Several hospitals and other institutions received large bequests from the estate of the late Mrs. Marie Engert-Colman, who died in England recently. Among the bequests are the following: St. Peter's, St. Catherine's, Brooklyn, Wyckoff Heights, Long Island College hospitals, Brooklyn, and Mary Immaculate Hospital, Jamaica, and St. Vincent's Hospital, New York, \$30,000 each; St. Mary's Hospital, \$50,000 and the proceeds from the sale of jewelry; Faith Home for Incurables, Visiting Nurse Association of Brooklyn, House of St. Giles the Cripple, Brooklyn Home for Consumptives, \$25,000 each.

Faculty Changes at Columbia.—Dr. Alphonse Raymond Dochez, John E. Borne professor of medical and surgical research, Columbia University College of Physicians and Surgeons, has been appointed executive officer of the department of bacteriology, according to *New York Medical Week*. Dr. Dochez succeeds the late Dr. Frederick P. Gay. Dr. LeGrand H. Hardy has been made assistant clinical professor of ophthalmology and Dr. Solomon Biloon promoted to assistant clinical professor of medicine. Mary Swartz Rose, Ph.D., professor of nutrition, will retire July 1, 1941, after a year's leave of absence. Dr. Rose is a member of the Council on Foods and Nutrition of the American Medical Association.

Dysentery on Refugee Ship.—Thirty-six cases of a mild bacillary dysentery were found on the *S. S. Washington* when she arrived from Galway, Ireland, July 13, bringing Americans from the war zones. The illness was limited to the tourist class, in which there were 829 passengers. When inspectors from the health department reached the boat seven who apparently recovered had disembarked, but twenty-nine who were still ill remained aboard. As these recovered at intervals they were allowed to disembark, but seven were still aboard July 15, according to *New York Medical Week*. The health department followed up all passengers living in New York and notified state health departments concerning those who lived elsewhere. An epidemiologic investigation was being made.

NORTH CAROLINA

Society News.—Dr. Frank Wood, Marion, among others, addressed the Thermal Belt Medical Society, Saluda, July 11, on "Prophylactic Use of Sulfanilamide."—At a meeting of the Catawba Valley Medical Society, July 11, the speakers were Drs. Frank W. Jones, Newton, on "Management of Some Chest Injuries"; Franklin C. Smith, Charlotte, "Fallacies in Ophthalmology," and John W. Ervin, Morganton, who reported a case of thrombopenia with leukemia of unknown origin.—Mr. John Elliott, Salisbury, addressed the Forsyth County Medical Society, Winston-Salem, June 18, on "The Use of Plasma as a Substitute for Whole Blood."—Dr. Samuel F. Ravenel, Greensboro, addressed the Buncombe County Medical Society, Asheville, July 15, on "Complications of Acute Hemorrhagic Nephritis in Children." Dr. Samuel M. Bittinger, Black Mountain, was the speaker July 1 on "Nontuberculous Diseases of the Lung."

Personal.—Dr. Wingate M. Johnson, Winston-Salem, received the honorary degree of doctor of science at the recent commencement at Wake Forest College.—Dr. William L. Patman, Greensboro, has been appointed general director of Chatham Hospital, Siler City.—Dr. Wilfred N. Sisk, recently on the staff of the Venereal Disease Medical Center, U. S. Public Health Service, Hot Springs National Park, Ark., has been appointed health officer of Buncombe County to succeed the late Dr. Howard L. Sumner.—Dr. Robert L. Russell, the chief of the tuberculosis and general medical service at the Veterans Administration Facility, Oteen, retired from the service recently, it is reported. He will reach the age limit in

September.—Charles D. Van Cleave, Ph.D., formerly instructor of anatomy, Cornell University Medical School, has been appointed assistant professor of anatomy at the University of North Carolina School of Medicine, Chapel Hill.

OHIO

New State Laboratory.—The state emergency board has set aside \$50,000 for a new laboratory building for the state department of health in Columbus. It will be erected on the campus of Ohio State University and marks another step toward the goal of state and university officials to concentrate all health department facilities on the campus. According to the state medical journal, the project calls for a \$350,000 building, of which the new laboratory structure will be one wing, but construction of the whole unit must await legislative appropriation. At present most of the health department's laboratory facilities are in an old building on the campus, which will be dismantled after their removal. Because of lack of space the laboratories for the division of industrial hygiene are now in a rented office building in downtown Columbus. All offices of the health department except the laboratories are now located on the third floor and in the basement of the State Office Building.

PENNSYLVANIA

Personal.—Dr. Everett S. Barr has resigned as medical director of the Chester County Hospital, West Chester, it is reported.—Dr. Ralph Lee Hill, medical superintendent of the Wernersville State Hospital, received the honorary degree of doctor of science at the recent commencement of Franklin and Marshall College, Lancaster.

Society News.—Dr. Paul A. Keeney, Harrisburg, was named president-elect of the Pennsylvania Public Health Association at the recent annual meeting and Mr. Harold H. Keller, Philadelphia, became president. Dr. John J. Shaw, state secretary of health, Harrisburg, is honorary president.—Dr. Joseph H. Barach, Pittsburgh, addressed the Warren County Medical Society, Warren, July 8, on "The High Carbohydrate Diet and Newer Insulins in the Treatment of Diabetes."—Dr. Charles B. Daugherty, Tyrone, addressed the Blair County Medical Society, June 25, in Altoona on national mobilization and defense.—Dr. Carl E. Ervin, Harrisburg, addressed the Medical Society of Franklin County, June 18, on "Disorders of the Thyroid."

Philadelphia

Dr. Riesman's Bequests.—Dr. David Riesman, who died June 3, ordered in his will that his brain be given to the Wistar Institute of Anatomy for research purposes, according to a newspaper report. Among several charitable bequests were \$1,000 to the College of Physicians of Philadelphia; \$500 to the Philadelphia County Medical Society and \$2,000 to the medical board of the Philadelphia General Hospital "to encourage research on the part of the staff—not a prize but a stipend."

The Bicentennial Conference.—The University of Pennsylvania will hold a conference on medical, natural and social sciences, fine arts, humanities and religion, September 16-20, as part of the observance of the two hundredth anniversary of the founding of the university. The program on the medical sciences will consist of one address each morning, followed by symposiums. Those who will give the addresses, according to the preliminary program, are:

Dr. Thorvald Madsen, director of the State Serum Institute, Copenhagen, Denmark, subject to be announced.

Dr. Lawrence J. Henderson, Abbott and James professor of chemistry, Harvard Medical School, Boston, The Study of Man.

Dr. Everts A. Graham, Bixby professor of surgery, Washington University School of Medicine, St. Louis, Two Centuries of Surgery.

William Mansfield Clark, Sc.D., De Lamar professor of physiological chemistry and director, department of physiological chemistry, Johns Hopkins University, Baltimore, A Challenge to Scholarship.

The symposiums will cover the following topics: problems and trends in virus research, therapeutic advances in psychiatry, medical problems of old age, nutrition, female sex hormones, hypertension, genesis of cancer, dental caries, development of occlusion, problems of intestinal obstruction, the relation of diseases in lower animals to human welfare, modern aspects of the antituberculosis program, chemotherapy, the university and public health statesmanship. More than fifty speakers will take part in these discussions. On Friday, September 20, there will be an alumni meeting, followed by a special convocation to be attended and addressed by the President of the United States. On Saturday, September 21, officials of the university will hold a reception for official delegates to the conference, and this will be followed by the bicentennial convocation, at

which honorary degrees will be conferred on a group of scholars. Inquiries about any of the proceedings during the Bicentennial Celebration should be addressed to the Registrar of the Bicentennial Conference, University of Pennsylvania, Philadelphia.

TENNESSEE

Society News.—The Dyer, Lake and Crockett Counties Medical Society, Dyersburg, was addressed recently by the following Memphis physicians: Drs. Harwell Wilson, diagnosis and management of thyroid disease; Robert L. Sanders, dyspepsia; Robert Lyle Motley, hypertension; Raphael Eustace Semmes, surgical aspects of hypertension, and Thomas D. Moore, renal aspects of hypertension.—Dr. William H. Enneis addressed the Knox County Medical Society, Knoxville, recently on undulant fever.—Drs. Joseph H. Francis and Joseph A. Crisler, Memphis, addressed the Madison County Medical Society recently on "Treatment of Duodenal Ulcer" and "Management of Various Types of Goiter" respectively.—Speakers at a meeting of the Washington County Medical Society recently were Drs. Horace B. Cupp, Mountain Home, on "Spinal Anesthesia"; Wallace L. Poole, Johnson City, and Carroll H. Long, New Orleans, "Use of Pentothal Sodium as an Intravenous Anesthetic."

UTAH

State Medical Meeting in Ogden.—The annual meeting of the Utah State Medical Association will be held in Ogden, August 29-31, with the Weber County Medical Society celebrating its fiftieth anniversary as a special feature. The program includes the following guest speakers:

Dr. James Dewey Bisgard, Omaha: Treatment of Carcinoma of the Bowel; Recent Advances in Surgery.

Dr. James G. Carr, Chicago: Obscure Fever; Clinical Diagnosis of Coronary Occlusion.

Dr. James F. Churehill, San Diego: Diagnosis and Management of Heart Irregularities; Congestive Heart Failure.

Dr. Herbert E. Coe, Seattle: Congenital Defects—A General Survey and Prognosis; The Bearing of Growth and Development on Children's Surgery.

Dr. Fred J. Hodges, Ann Arbor, Mich.: Titles to be announced.

Dr. Verne C. Hunt, Los Angeles: Surgical Significance of Gastrointestinal Bleeding; Obstructing Lesions of the Common Duct.

Dr. Joseph E. J. King, New York: Oxycephaly; Brain Abscess.

Dr. Paul B. Magnuson, Chicago: Fractures of the Neck of the Femur, Both Recent and Ununited; Relief of Certain Types of Arthritis by Surgery.

Dr. James T. Priestley, Roebester, Minn.: Conservative Surgical Treatment of Staghorn Renal Calculi; Carcinoma of the Bladder with Particular Reference to Total Cystectomy.

Dr. John E. Raaf, Portland, Ore.: Diagnosis and Treatment of Late Effects of Head Injuries; Treatment of Patients with Protruded Intervertebral Disks.

WISCONSIN

Society News.—Dr. Henry L. Greene, Madison, addressed the Jefferson County Medical Society, June 20, in Jefferson on "Epiphyseal Injuries in Children."—Dr. Sumner L. S. Koch, Chicago, addressed the Brown-Kewaunee-Door Counties Medical Society, Green Bay, June 11, on "Injuries, Infections and Deformities of the Hand."—Drs. Hugh F. Ringo and Mark W. Garry, Montreal, addressed the Ashland-Bayfield-Iron Counties Medical Society, June 26, in Ironwood on prevention of silicosis in iron miners.—Speakers before the Trempealeau-Jackson-Buffalo Counties Medical Society in Galesville, July 18, were Drs. Walter G. Sexton and Lyman A. Copps, Marshfield, on "Hematuria" and "Interesting Eye Conditions" respectively.

GENERAL

Missing Physician Found.—Dr. Runyon H. Irvin, Mount Vernon, Ill., reported recently to be missing from home, was found in a hospital in Newark, N. J. He had been injured when a heavy sliding door struck him. Identification was established through an announcement of Dr. Irvin's disappearance in THE JOURNAL, July 27, page 312.

Board of Anesthesiology Increases Fees.—The American Board of Anesthesiology announces that on account of increased administrative expenses it has been necessary to increase the application and administrative fees. The new fees are \$25 with application and \$50 before examination. In case of rejection, all fees paid will be refunded except a \$10 filing fee (before full examination). These new fees go into effect Jan. 1, 1941. If application is filed before that time, the rate of \$50 (\$5 for registration, not returnable, and \$45 examination fee) still applies. Dr. Paul M. Wood, 745 Fifth Avenue, room 1503, New York, is secretary.

Opening for Superintendent of Hospitals.—The Civil Service Commission, Minneapolis, announces an opening for the position of superintendent of hospitals. Applications may be

obtained from the commission at room 109, City Hall, Minneapolis. The examination will be open to citizens of the United States who have been residents of the United States for at least one year immediately preceding the date of closing of applications, September 11. Candidates must not have reached their fifty-fifth birthday and must be graduates of a recognized medical school with at least ten years of successful experience as a physician, surgeon or medical executive. This experience shall include five years as an administrator or superintendent in an accredited hospital of a capacity of at least fifty beds, or three years as an administrator, superintendent or assistant superintendent in an accredited hospital with a bed capacity of at least 200, or one year in these positions in an accredited hospital with at least a 500 bed capacity. The salary will be \$5,000 annually with living quarters or \$6,000 without quarters.

Clinic on Health in Industry.—The Muskegon Employers Association, the Employers Association of Grand Rapids and the National Association of Manufacturers sponsored a clinic on health in industry at the Occidental Hotel, Muskegon, Mich., June 28. The program included:

The Meaning and Value of Industrial Health, as analyzed by the state health department, Dr. Kenneth E. Markuson, Lansing, director, Michigan Bureau of Industrial Hygiene; as evaluated by the state medical society, Dr. Henry Cook, Flint, chairman, Michigan Committee on Occupational Disease and Industrial Hygiene; as experienced by the manufacturer, Mr. H. M. Taliaferro, president, American Seating Company.

Organization and Costs of an Industrial Health Service, Dr. Constant M. Colignon, Muskegon, Mich., medical director, Campbell, Wyant and Cannon Foundry Company.

A Plant Health Program and Public Relations, Mr. Ralph L. Lee, department of public relations, General Motors Corporation.

Dr. Victor G. Heiser, New York, consultant, committee on healthful working conditions, National Association of Manufacturers, addressed a luncheon session on "Industrial Health and National Defense."

Society News.—Dr. Fred H. Albee, New York, was elected president of the International College of Surgeons at a meeting in Philadelphia in June. The United States chapter and the governing council decided to transfer headquarters of the organization from Geneva to Washington for the duration of the war. Dr. Desiderio A. Roman, Philadelphia, was elected president of the United States chapter.—Dr. Matthew C. Riddle, Portland, Ore., was named president-elect of the Pacific Northwest Medical Association at its annual meeting in Spokane, Wash., July 12, and Dr. Donald A. Palmer, Spokane, was installed as president. State councilors were elected as follows: Drs. Orval F. Swindell and Everett N. Jones, Boise, Idaho; Arthur J. Movius, Billings, Mont.; Howard P. Kirtley and Emerson F. Root, Salt Lake City, Utah; Doyle Joslin, Rock Springs, and Herbert L. Harvey, Casper, Wyo. The next meeting also will be held in Spokane.—Col. Harold W. Jones, librarian of the Army Medical Library, Washington, D. C., was reelected president of the Medical Library Association at its annual meeting in Portland, Ore., June 25-27. Dr. Robert E. Schlueter, St. Louis, was elected vice president and Miss Anna C. Holt, Harvard Medical School Library, Boston, was reelected secretary. The 1941 convention will be held at the University of Michigan Medical School, Ann Arbor.

Fatal Accidents.—The U. S. Bureau of the Census recently released a statistical study of fatal accidents in the six years 1933 to 1938. The report shows that in 1933 fatalities from accidents totaled 90,932 and thereafter the number increased to a high point of 110,052 in 1936. Then it decreased to 93,805 for 1938. Special emphasis was placed on deaths caused by fires, which ranked seventh among all accidental causes from 1933 to 1938 and advanced to sixth place in 1938. Figures for the years in succession were 1,521 in 1933, 1,752 in 1934, 1,581 in 1935, 1,913 in 1936, 1,688 in 1937 and 1,650 in 1938. Fire claimed more victims in the age group 5 to 9 than in any other group in 1938; there were 129 deaths in this group, which was 7.8 per cent of all persons burned to death. The next largest number was in the group 50 to 54, with 109 deaths. Age distributions for different types of fatal accidents vary greatly, the report showed. Only 18.3 per cent of deaths from injury by fall occurred among persons under 45 years old, who constitute 77 per cent of the population; but 55.8 per cent of the automobile fatalities and 91.3 per cent of the air transportation accidents were in this younger group. The report includes several tables indicating the accident fatalities for individual states and for cities with a population of 100,000 or more. It tabulates for all types of accidents the number of deaths, the death rate per hundred thousand of estimated population, the percentage of all deaths from accidents and the rank-order frequency among the different types of accidents.

LATIN AMERICA

Society News.—The Second National Medical Congress in Peru is to be held this month in Arequipa under the auspices of the Peruvian government in connection with the celebration of the four hundredth anniversary of the founding of the city. There will be four sections: medicine, surgery, hygiene and social medicine, and specialties.—The First Cuban Congress of Regional Pathology, Social Medicine, Preventive Medicine, Public and Private Hygiene was recently held with Dr. Juan de Moya Flamand, secretary of health and welfare, as president. The congress studied problems relating to the diseases peculiar to Cuba in connection with environments of each region, methods of eradicating them and methods of disseminating information on hygiene and sanitation.—Dr. Ramon Castroviejo, New York, addressed the Society of Ophthalmology of São Paulo, Brazil, recently on "Surgery of the Cornea." He was also honored by a banquet given by the society.

FOREIGN

Prize Offered for Essay in Ophthalmology.—The Ophthalmological Society of the United Kingdom announces the Treacher Collins Prize, which is awarded triennially for the best essay on a subject chosen by the council of the society. The prize is open to qualified medical practitioners of any nationality but must be written in English. The subject is "Allergy of the Eye and Its Adnexa." Essays should be submitted before December 31 to the honorary secretary, Ophthalmological Society of the United Kingdom, 5 Racquet Court, Fleet Street, London, E. C. 4. Names should not be on the essay but a distinguishing pseudonym or quotation, which should also be on a sealed envelop containing the candidate's name and address to accompany the essay.

CORRECTIONS

Sarcoidosis.—The first bibliographic reference in the editorial "Sarcoidosis" in THE JOURNAL, July 27, should read the *New England Journal of Medicine* instead of the *British Journal of Dermatology*.

Morphine Derivative in Massive Doses.—In THE JOURNAL, July 20, page 259, there appeared an abstract entitled *Morphine Derivative in Massive Doses*. The drug in question, known as Eupaverine, is 1-(3,4-methylenedioxybenzyl)-3-methyl-6,7-methylenedioxyisoquinoline and should be properly classified in the isoquinoline group of drugs obtainable from opium. The actions of members of this group of compounds differ in many respects from the phenanthrene group of drugs also obtainable from opium. It is the latter group which contains morphine and its derivatives.

Government Services

The Government Needs Physicians

The U. S. Civil Service Commission announces open competitive examinations to fill medical officer positions in the U. S. Public Health Service and the Food and Drug Administration, Federal Security Agency; Veterans' Administration; Civil Aeronautics Authority, Department of Commerce, and the Indian Service, Department of the Interior. The examinations cover three grades with salaries ranging from \$3,200 to \$4,600, subject to a deduction of 3.5 per cent toward a retirement annuity. Applications must be filed with the civil service commission, Washington, D. C., and will be received until further notice. Applicants must have graduated with an M.D. degree from a recognized medical school and must have had professional experience in one of the following optional branches: aviation medicine; cancer research; cardiology; dermatology; eye, ear, nose and throat (singly or combined); general practice; industrial medicine; internal medicine and diagnosis; medical pharmacology; neuropsychiatry; pathology; bacteriology and roentgenology (singly or combined); public health; surgery; tuberculosis, and urology. For some positions in the Veterans' Administration, applicants for associate medical officer need not have had experience other than one year of internship. Applicants for the associate grade must not have passed their fortieth birthday, and for the other two grades they must not have passed their fifty-third birthday. Announcements containing further information and the application forms may be obtained from the secretary of the board of U. S. Civil Service Examiners at any first or second class postoffice or from the U. S. Civil Service Commission, Washington, D. C.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 6, 1940.

The Evacuation of Dunkirk

The Emergency Hospital Service was established for dealing with the heavy casualties expected from air raids among the civilian population. The London area was divided into ten sectors, each with its apex in central London near one of the large hospitals (which would act as a casualty clearing station) and widening out to advanced bases and then to base hospitals 30 or 40 miles away, so as to be safer from bombing. No casualties have yet occurred in London, but the scheme has been put to its first test on a large scale by an emergency in which the stream of casualties came in the opposite direction to the expected one. In the days preceding the evacuation of Dunkirk 7,000 beds were made ready. From the hospital ships the most serious cases were taken to hospitals near the ports; the less severely wounded were sent by train to hospitals farther away. After the hospital ships came the smaller boats, each having some wounded to disembark. It was not known when the flow would stop and so arrangements were made to evacuate many of the less seriously wounded to hospitals still farther off in the west, with the result that the sector in use could comfortably have dealt with three times the number of casualties it was called on to handle. Actually 1,873 cases were treated in the sector hospitals in a period of twelve days. These included French, Belgian and British soldiers and sailors and a few refugees. Although nearly half had received no treatment other than first aid and were carried in ambulances from 30 to 60 miles, only thirty-three (1.7 per cent) died. The response of the sector hospitals was wonderful. Not one was found to confess that it could not undertake more work. Every one made it a point of honor to see that everything possible was done for the incoming wounded with the maximum of speed. As the work increased, mobile surgical teams were sent from London and additional trained operating room nurses, house officers and student dressers were drafted into coastal towns that needed help.

Sulfathiazole in Staphylococcal Infections

At a meeting of the Section of Therapeutics and Pharmacology a discussion took place on the use of sulfathiazole, particularly in staphylococcal infections. Mr. E. C. Butler said that staphylococcal septicemia was much more common and fatal than was generally supposed. Every death from osteomyelitis and nearly every death from cavernous sinus thrombosis and many deaths from boils, carbuncles and infected fingers could be attributed to *Staphylococcus aureus*. Any treatment to be effective must be started at the beginning of the disease. At the London Hospital every patient with a severe staphylococcal infection was given 20,000 units of antitoxin. It was also necessary to find a drug which may help to destroy staphylococci. The sulfonamides did not affect the course of the severe cases. Staphylococcal infections were far more difficult to treat than hemolytic streptococcus infection. He had found sulfathiazole of little or no effect on a staphylococcal infection when the blood culture was positive. But it might be of benefit after the source of the bacteria had been removed or when the lesion was localized, as in carbuncle or cellulitis. But it must be given early, and surgical treatment and antitoxin must not be neglected. The results so far did not support the optimistic reports from America.

Dr. George Melton reported five cases of osteomyelitis and five of carbuncle of the face treated with sulfathiazole. The first case, an acute osteomyelitis of the radius and ulna after

open reduction of a fracture, improved but did not clear up under sulfapyridine. Sulfathiazole was then given to a total dosage of 26 Gm. After each injection the patient complained of headache and vomited, but marked improvement took place under the sulfathiazole. In a case of acute osteomyelitis of the lower end of the humerus, pyrexia persisted after the administration of sulfathiazole but subsided on drainage of a subperiosteal abscess. The third case, acute osteomyelitis of the upper end of the femur, cleared up under sulfathiazole. The fourth case, affecting the lower end of the femur, showed pyrexia after drainage, which subsided under sulfathiazole. In the fifth case there was acute osteomyelitis of the ilium and suppurative arthritis of the hip. Blood culture yielded *Staphylococcus aureus*. No improvement followed sulfathiazole, the blood culture remaining positive. Of the five cases of carbuncle, recovery under sulfathiazole occurred in four and the fifth was still under treatment. Melton's experience was that large doses of sulfathiazole were necessary to achieve results comparable with those of sulfapyridine, but he was not prepared to make any comparison between the two drugs.

Indications for Removal of Tonsils and Adenoids

A reaction has taken place against operations for removal of tonsils and adenoids, which reached their peak about 1930. Thus in the Hospital for Sick Children, London, 4,730 operations were performed in that year, while in 1938 the number had fallen to 2,729. In opening a discussion at the Royal Society of Medicine on the Indications for Removal of Tonsils and Adenoids, Sir Lancelot Barrington-Ward said that the tonsil was in his experience much the more dangerous element. Its structure allowed organisms to lie dormant, to remain moderately but continuously active, leading to chronic general poisoning or flare-up into acute inflammation at indefinite intervals. Adenoids, on the other hand, acted only mechanically by obstructing respiration or by a low grade infection causing inflammation of the ear or cervical glands. The importance of adenoids was greatest in the earlier years of life and they might require removal within the first few months. If present in later years, the tonsils were usually also infected and it was wise to deal with both.

What were the conditions of the tonsils which demanded operation? The most usual description given was that they were large and septic, but the combination was not constant. Large tonsils might not be septic and septic tonsils might not be large. Mere size was not an indication for removal of a tonsil unless by reason of size it was injuring the patient. Sometimes a persistent cough might justify operation. More commonly there was obstruction to the food and air passages. A septic tonsil was a menace and should always be removed. How was it to be decided that a tonsil was septic? A standard appearance that would satisfy every observer was impossible and bacteriologic examination was not always helpful. More could be learned from the secondary effects, which might be direct or indirect. Among direct effects were: 1. Repeated attacks of tonsillitis, the only certain way of stopping which was removal. 2. Chronic enlargement of the upper deep cervical lymphatic gland, without enlargement of other glands, which always indicated tonsillar infection; such a gland was likely to harbor the tubercle bacillus of bovine strain; in the treatment of tuberculous glands, removal of the tonsils was essential. 3. Otitis media, with its sequels mastoiditis and deafness, which in the majority of cases were the result of infected tonsils and adenoids. Here a great advance of recent years was continuous medical supervision of school children and early treatment of the source of infection.

Indirect effects were less certain grounds on which the tonsil could be held responsible. In some it could be blamed only as a port of entry of a specific organism. To remove the

tonsil after the damage had been done was like shutting the stable door after the horse had been stolen. Tonsillectomy was reasonable only if there appeared to be continued infection or reinfection. Rheumatism with associated heart disease and chorea was a good example. The responsibility of selection here lay mainly with the physician. Chronic sepsis might have a wider effect. In a flabby child with scoliosis, knock-knee or valgus, chronic infection of the tonsils was not uncommon and the first part of the orthopedic treatment must be elimination of the toxemia. The least definite indication and perhaps the one that has brought most disappointment to the operator was recurrent or persistent nasopharyngeal catarrh and the common cold. If every cold began with a sore throat, removal of the tonsils might prevent further attacks. This was successful in the majority of cases, and if the colds returned they were less severe; but the wise surgeon would give no guaranty of immunity.

BUENOS AIRES

(From Our Regular Correspondent)

July 1, 1940.

Broadcasting of Health Programs

The national department of public health has recently organized popular radio lectures on the problems with which its various divisions deal. These lectures are delivered, generally by the heads of these divisions, over the government broadcasting stations. The first program for the month of June lists as topics milk and nutrition, maternal care and the work of the division of maternal and child welfare service, illegal practice of medicine, prophylaxis against influenza, the national department of health and drug addiction, functions of the health department, cooperation of parents with the eugenic program of the state, occupational diseases and accidents, hypertrophy and tonsillar infections, the public and the medical profession, significance of medical examinations in early infancy, and pertussis.

Malaria Control

Malaria control in Argentina is directed by a division of the national department of public health, with its seat in Tucumán. Dr. Carlos Alberto Alvarado, its director, was formerly general secretary of the national health department. Malaria in Argentina is not a problem of swamps but is endemically established in areas at the foot of mountains and occasionally in mountainous territory. The province of Buenos Aires with its long low littoral is free from malaria. Different species of *Anopheles* are found in the low coastal lands but they do not attack man. *Anopheles pseudopunctipennis* is the chief disseminator of malaria. The first efforts of the malaria control division were the draining of stagnant waters until it was discovered that swamps bred only mosquitoes harmless to man. While other species of *Anopheles* prefer to breed in quiet shady waters with luxuriant vegetation, *Anopheles pseudopunctipennis* seeks the banks of rivers and brooks exposed to light and air that produce weeds (algae *spirogyrae*) which are indispensable food to the malaria breeding variety. Paradoxically, drainage canals create dangerous breeding places. Waters with banks devoid of vegetation are found to breed the weeds favored by the malarial *anopheles*. These aquatic plants are easily crowded out by taller plants of more luxuriant growth but thrive where they have no overpowering competition. Along the course of drainage canals the algae *spirogyrae* thrive until stronger plants displace them. Canals built up with stone or cement were observed to prevent the ranker vegetation and thus furnished good harbor to the algae that bred the disease carriers. For this reason, needless clearing of drainage canals is also inadvisable as it attacks the more luxuriant plant growth. Cress such as *Cardamina flaccida* and burdock (*Senecio creameplorum*) set out to combat algae *spirogyrae* suffer from the disadvantage that rising water may kill them off.

Whether artificially watered rice plantations promote *anopheles* development has so far received no satisfactory answer. International observations seem to be contradictory. Alvarado conducted investigations in Tucumán and other northern provinces in which rice is grown. He found that irrigated rice fields were strongly favorable to the *anopheles* in question. On spleen examination the hematologic index of people living near the rice fields was higher than that of those living farther away. In regions infested with malaria a systematic "policing" of centers of infestation has been organized. Maps indicate the spots that are to be attacked. The species of *Anopheles* found in these regions is identified. Twice a year a general test is made, by means of the hematologic index, of infants 2 years old and younger native to the region. The index for the "epidemic type" is taken during April and May. This indicates the maximum level of malaria infection, that is, new and old infections. The index of the "endemic type" is taken in October and November. It indicates only the chronic infections. The age level of 0 to 2 was selected to make sure that the disease was not contracted elsewhere and because the presence of malaria parasites is best determined at this age. Tests made in one community in Tucumán based on 200 specimens resulted in 14.5 per cent positive reactions in October 1936. Subsequent tests gave a 5 per cent reaction in April 1937 and 1.5 per cent in October 1937. In one year malaria had been reduced by 90 per cent. The total malaria-infested area of Argentina is estimated at 120,000 square kilometers with 850,000 inhabitants. At present only 1,200 square kilometers has been given attention.

The annual report of the malaria control division of the national public health department for 1939 indicates that malaria incidence was within normal limits and showed a tendency to decline. Tertian malaria preponderated. More than 120,000 persons were treated. According to Alvarado's observations the frequency of congenital malaria is enormous. Several full-time positions have been created and three (of six) regional directors appointed.

Personals

Dr. Francis Scott Smyth of the pediatric department of the University of California has arrived in Buenos Aires for six months of research activity with Prof. B. A. Houssay.

Dr. Hernán Aguilar, associate professor at the faculty of medicine of Buenos Aires, has sailed for the United States to do research work at Washington University, St. Louis, on thoracic surgery.

Marriages

FRANK TURNER NORRIS, A. A. Surg. Lieut. (j. g.) U. S. Navy, Portsmouth, Va., to Miss Courtney Louise Taylor of Norfolk, May 24.

GALEN GLICK CRAUN, Huntington, W. Va., to Miss Beulah Genevieve Spencer of Richmond, Va., June 21.

GEORGE MILTON ROBINS, Louisville, Ky., to Miss Mary Frazier Kimbrough of Lexington, June 22.

CECIL CURTIS COLLINS JR., Jacksonville, Fla., to Miss Marjorie Winston of Durham, N. C., June 4.

EUSTACE VITOL CHAUVIN JR., Lafayette, La., to Miss Vanola Bailey of Austin, Texas, in June.

EMMETT STEVENSON LUPTON, Raleigh, N. C., to Miss Mary Paschal of Wake Forest, June 4.

EDWARD H. SIBLEY, Sioux City, Iowa, to Miss Clara Marie Munger of Grinnell, June 22.

FORREST ELLIOTT OGLESBY to Miss Mildred Virginia Garret, both of Norfolk, Va., June 8.

JOHN L. KLEIN JR., Muscatine, Iowa, to Miss Beatrice Kaiser of St. Paul, June 17.

JOHN A. LINEBERRY to Miss Jane Elizabeth Lassiter of Four Oaks, N. C., June 4.

Deaths

Joseph Williams Schereschewsky ♂ Medical Director, United States Public Health Service, Boston; Dartmouth Medical School, Hanover, N. H., 1899; veteran of the Spanish-American War; in 1899 was appointed assistant surgeon in the United States Public Health Service and was promoted through the grades to that of medical director in 1930; from 1913 to 1918 was in charge of field investigations of occupational diseases; from 1918 to 1922 was assistant surgeon general in charge of the division of scientific research; was in charge of cancer investigations from 1922 to 1937; established a cancer research center at the Harvard Medical School in Boston; in 1935 was awarded the Distinguished Service Key of the American Congress of Physical Therapy; in 1937 organized the cancer control program for the state of Georgia; past president of the American Association of Industrial Physicians and Surgeons; member of the House of Delegates of the American Medical Association from 1918 to 1922; aged 67; died, July 9, at his summer home in West Harwich, Mass., of angina pectoris.

John Alexander Lanford ♂ New Orleans; Medical College of Alabama, Mobile, 1905; instructor of anatomy at his alma mater from 1908 to 1910; instructor of surgical pathology from 1911 to 1914 and assistant professor of pathology and bacteriology at the Tulane University of Louisiana School of Medicine since 1914; past president of the Orleans Parish Medical Society; member of the American Association of Pathologists and Bacteriologists and the American Society of Clinical Pathologists; member of the board of directors of the American Society for the Control of Cancer; fellow of the American College of Physicians; served during the World War; aged 59; pathologist to the New Orleans Hospital and Dispensary for Women and Children; consulting pathologist to the United States Marine Hospital; director of laboratories and pathologist to the Touro Infirmary, where he died, July 2, of coronary thrombosis.

Edwin Pakenham Ruggles ♂ Boston; Boston University School of Medicine, 1900; at various times lecturer, instructor, assistant professor, associate professor, professor and professor emeritus of obstetrics at his alma mater; member of the New England Obstetrical and Gynecological Society; fellow of the American College of Surgeons; consulting obstetrician to the Massachusetts Memorial Hospitals; served during the World War; aged 67; died, June 19, of cirrhosis of the liver.

Laurence Burton Sisson ♂ Auburn, N. Y.; Syracuse University College of Medicine, 1912; served during the World War; on the staffs of the Auburn City Hospital and the Mercy Hospital; past president of the Cayuga County Medical Society; formerly physician in charge of the Auburn State Prison Hospital; aged 50; died, June 17; at the Strong Memorial Hospital, Rochester, of carcinoma of the bladder.

Martin Thomas Powers ♂ Utica, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1905; member of the American Roentgen Ray Society and the Radiological Society of North America, Inc.; past president of the Utica Academy of Medicine; chairman of the New York State Roentgenology Society; aged 60; on the staffs of the Utica General Hospital and St. Elizabeth Hospital, where he died, June 14, of coronary thrombosis.

William Arthur Harvie, Regina, Sask., Canada; University of Toronto Faculty of Medicine, 1908; fellow of the American College of Surgeons; past president of the Saskatchewan Medical Association; on the staffs of the Regina General and Regina Grey Nuns' Hospital; surgical consultant, department of pensions and national health; served during the World War; aged 54; died, May 31.

Claude Burgess Williams, Elizabeth City, N. C.; University College of Medicine, Richmond, Va., 1903; member and formerly vice president of the Medical Society of the State of North Carolina; county health officer; at one time a trustee of the Agricultural and Mechanical College, Raleigh; formerly member of the local school board; aged 62; died, June 21, of cerebral hemorrhage.

B. Vernon Dickson, Covington, Tenn.; Memphis (Tenn.) Hospital Medical College, 1901; member of the Tennessee State Medical Association; past president and secretary of the Tipton County Medical Society; aged 63; died, June 30, in the Baptist Hospital, Memphis, of pleurisy with effusion, cardiac insufficiency and chronic tuberculosis of the lungs.

William James Vivian, Northport, N. Y.; Dartmouth Medical School, Hanover, N. H., 1912; member of the Massachusetts Medical Society, American Psychiatric Association and

the New England Society of Psychiatry; on the staff of the Veterans Administration Facility; aged 55; died, June 10, of coronary thrombosis.

Edward Allen Pease ♂ Pasadena, Calif.; Harvard Medical School, Boston, 1892; member of the Massachusetts Medical Society; formerly surgeon to the Boston Dispensary, Free Hospital for Women, Brookline, and the Carney Hospital, Boston; aged 75; died, June 19, of bronchopneumonia.

William A. Beach, Mankato, Minn.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1893; member of the state board of medical examiners in 1906; formerly mayor of Mankato; aged 71; died, June 12, of cerebral hemorrhage.

Marie Olivier Becnel, New Roads, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1896; member of the Louisiana State Medical Society; for many years parish coroner; aged 66; died, June 26, of cerebral hemorrhage and arteriosclerosis.

Charles Edward Long, Williamsville, N. Y.; University of Buffalo School of Medicine, 1891; served during the World War; for many years county medical examiner; aged 70; died, July 4, in the General Hospital, Buffalo, of acute gangrenous appendicitis.

Murvington Emery Malaun, Carbondale, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1896; member of the Medical Society of the State of Pennsylvania; aged 72; died, June 25, of injuries received in an automobile accident.

Thomas J. O'Malley, Chicago; College of Physicians and Surgeons of Chicago, 1896; member of the Illinois State Medical Society; served during the World War; formerly member of the board of education; died, June 19, of myocarditis.

William J. Harlan ♂ Bartlett, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1898; for many years president of the school board; aged 65; died, May 2, in a hospital at Temple of coronary thrombosis.

J. Sidney Hoffa, Williamsport, Pa.; Medico-Chirurgical College of Philadelphia, 1903; member of the Medical Society of the State of Pennsylvania; aged 60; died, June 12, in the Williamsport Hospital of pontile hemorrhage.

Russel Clark Paris, Hudson Falls, N. Y.; Regents of the University of the State of New York, 1883; member of the Medical Society of the State of New York; aged 80; died, June 16, of uremia and cerebral hemorrhage.

Roger Talmage Fox, Gloucester City, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1915; served during the World War; aged 51; died, June 22, in Florence of myocarditis and cirrhosis of the liver.

Joseph Goodman Knapp, Wyandotte, Mich.; Detroit College of Medicine and Surgery, 1915; served during the World War; on the staff of the Wyandotte General Hospital; aged 46; died, June 15, of encephalomyelitis.

Lorenzo Burton Zimmerman, Mount Carmel, Pa.; Jefferson Medical College of Philadelphia, 1894; member of the Medical Society of the State of Pennsylvania; aged 69; died, June 20, of coronary thrombosis.

Nelson A. Ludington, New Haven, Conn.; Yale University School of Medicine, New Haven, 1901; member of the Connecticut State Medical Society; aged 61; died, June 26, of hypertension and coronary occlusion.

George Hayward Coburn ♂ Rangeley, Maine; University of Pennsylvania Department of Medicine, Philadelphia, 1875; aged 85; died, June 18, of bronchopneumonia, arteriosclerosis and cerebral hemorrhage.

Fitz Henry Farrington, Boulder, Colo.; State University of Iowa College of Medicine, Iowa City, 1893; member of the Colorado State Medical Society; aged 77; died, May 17, of cerebral hemorrhage.

Allen Andrew Van Slyke, Mount Jewett, Pa.; University of Buffalo School of Medicine, 1882; member of the Medical Society of the State of Pennsylvania; aged 81; died, May 30, of angina pectoris.

Ralph Semmes Jackson ♂ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1900; aged 70; died, June 25, in the Nix Hospital of fracture of the left femur and lateral sclerosis.

Frederick Warren McCaw ♂ Colon, Neb.; John A. Creighton Medical College, Omaha, 1907; past president of the Saunders County Medical Society; aged 58; died, May 15, of heart disease.

Charles James Marquette, Nova, Ohio; Western Reserve University Medical Department, Cleveland, 1897; member of the county board of health; aged 69; died, June 20, of cerebral hemorrhage.

John Luke Hayden Ⓢ Louisville, Ky.; University of Louisville Medical Department, 1909; served during the World War; aged 51; died, June 25, in the Norton Infirmary of pulmonary tuberculosis.

Josiah Murch Stanley Ⓢ Northboro, Mass.; University of the City of New York Medical Department, 1884; school physician for many years; aged 80; died, June 4, of coronary thrombosis.

Fritzroy Farnsworth Pillsbury, Lowell, Mass.; Dartmouth Medical School, Hanover, N. H., 1909; member of the Massachusetts Medical Society; aged 55; died, June 18, in Saco, Maine.

Louis Valerio Ⓢ Cincinnati; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1911; served during the World War; aged 54; died, June 4, of coronary thrombosis.

Edward Colfax McCurdy, Shellman, Ga.; Atlanta College of Physicians and Surgeons, 1902; member of the Medical Association of Georgia; aged 70; died, June 2, of arteriosclerosis.

Charles Henry Beadles, Racine, Wis.; John A. Creighton Medical College, Omaha, 1915; served during the World War; aged 53; died, June 8, in St. Catherine's Hospital, Kenosha.

John Porter Ferguson, Springfield, Mo.; Barnes Medical College, St. Louis, 1895; member of the Missouri State Medical Association; aged 69; died, May 6, of cerebral hemorrhage.

George Washington Smallwood, Pepperell, Mass.; University of the City of New York Medical Department, 1887; aged 78; died, June 21, of uremia and prostatic obstruction.

John A. Houser, West Salem, Ill.; Eclectic Medical Institute, Cincinnati, 1882; also a pharmacist; aged 81; died, June 28, in Quincy of uremia and hypertrophy of the prostate.

Cornelius Howard Duvall, Fort Worth, Texas; Louisville (Ky.) Medical College, 1901; served during the World War; aged 70; died, June 29, of acute pulmonary tuberculosis.

Clarence Hamilton Morris, Windsor, N. S., Canada; McGill University Faculty of Medicine, Montreal, Que., 1897; served during the World War; aged 67; died, May 22.

Jesse Thaxton Hayes, Oliver Springs, Tenn.; University of Nashville Medical Department, 1901; aged 66; died, June 28, in a hospital at Knoxville of injuries received in a fall.

William Cocke Lyons, Surgoinsville, Tenn.; Louisville (Ky.) Medical College, 1888; formerly bank president and member of the state legislature; aged 72; died, June 2.

John Clark Brown Ⓢ Wichita, Kan.; National University Medical Department, Washington, D. C., 1900; aged 81; died, June 25, of myocarditis, cholecystitis and liver abscess.

Welles James Lowry, Carbondale, Pa.; Jefferson Medical College of Philadelphia, 1882; member of the Medical Society of the State of Pennsylvania; aged 84; died, June 9.

Alexander Campbell, St. John's, Newfoundland; McGill University Faculty of Medicine, Montreal, Que., 1902; F.R.C.S., Edinburgh, Scotland, 1910; aged 64; died, May 16.

Samuel Jacob Fryer, Muskogee, Okla.; Hospital College of Medicine, Louisville, Ky., 1902; member of the Oklahoma State Medical Association; aged 63; died, June 19.

John Abner Hawkins, Danville, Va.; Medical College of Virginia, Richmond, 1918; member of the Medical Society of Virginia; aged 44; died, June 7, of pneumonia.

William Kepler Parker, Dix, Ill.; College of Physicians and Surgeons, Keokuk, Iowa, 1883; member of the Illinois State Medical Society; aged 89; died, June 7.

Robert C. Sheetz Ⓢ Orrick, Mo.; St. Louis College of Physicians and Surgeons, 1890; served during the World War; aged 73; died, May 25, of coronary occlusion.

Charles U. Patterson, Houston, Texas; Kentucky School of Medicine, Louisville, 1892; member of the State Medical Association of Texas; aged 76; died, June 6.

Caspar Wistar Miller, Wallingford, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1894; aged 71; died, June 24, of cardiorenal disease.

William Varner Wilcox, Sacramento, Calif.; California Medical College, San Francisco, 1899; aged 61; died, June 5, of chronic nephritis and heart disease.

Joseph Frank Mayes Ⓢ St. Louis; Washington University School of Medicine, St. Louis, 1904; aged 62; was found dead in bed, June 27, of heart disease.

Ernest Druecilla Burden, Brookline, Mass. (licensed in Massachusetts in 1895); aged 65; died, June 9, of cerebral hemorrhage and arteriosclerosis.

Stephane Dulude, Dassel, Minn.; School of Medicine and Surgery of Montreal, Que., Canada, 1898; aged 66; died, May 12, of coronary thrombosis.

Cecile Lenore Greil, Los Angeles; Eclectic Medical College of the City of New York, 1910; aged 67; died, June 11, of hypostatic pneumonia.

G. Cloud Eshelman, Portland, Ore.; Hahnemann Medical College and Hospital, Chicago, 1890; aged 81; died, June 26, of cerebral hemorrhage.

Elmer Ellsworth Stone, Los Angeles; Cooper Medical College, San Francisco, 1890; aged 70; died, June 9, of carcinoma of the prostate.

Israel Baikovich, Chicago; Chicago Medical School, 1915; aged 65; died, July 8, in the Mother Cabrini Hospital of carcinoma of the prostate.

Ernest Henry Mercer, San Francisco; California Medical College, San Francisco, 1896; aged 72; died June 6, of carcinoma of the prostate.

Chester Walton Young, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1913; aged 52; died, June 16, of carcinoma.

Alma Sophia Larson Goude, Minneapolis; College of Medical Evangelists, Los Angeles, 1918; aged 52; died, May 1, of carcinomatosis.

Gilbert La Fayette Foster, Wolfville, N. S., Canada; University of the City of New York Medical Department, 1896; died, May 17.

Francisco Liano Parra, El Paso, Texas; Universidad de Guadalajara Facultad de Medicina, Mexico, 1923; aged 43; died in June.

Edgar J. Klotz, Allentown, Pa.; Jefferson Medical College of Philadelphia, 1886; aged 76; died, June 8, of acute coronary thrombosis.

John Hund, Peoria, Ill.; College of Physicians and Surgeons of Chicago, 1887; aged 86; died, June 23, in St. Francis Hospital.

Harry Leo Devine, Springfield, Mass.; Baltimore Medical College, 1909; aged 56; died, June 29, in the Wesson Memorial Hospital.

Benjamin Robert White, Strasburg, Va.; University of Maryland School of Medicine, Baltimore, 1896; aged 69; died, June 21.

Herbert Clarence Bolstad, Pescadero, Calif.; University of Illinois College of Medicine, Chicago, 1913; aged 56; died, June 29.

Leopold Freiburger Ⓢ New York; University and Bellevue Hospital Medical College, New York, 1899; aged 72; died, June 2.

A. Le Grand Runion, Canonsburg, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1888; aged 89; died, June 11.

George Washington Hoglan, Bedford, Va.; Cincinnati College of Medicine and Surgery, 1885; aged 79; died, June 5.

Joseph L. Bennett, Kearney, Neb.; Eclectic Medical Institute, Cincinnati, 1874; aged 90; died, June 16, of acute nephritis.

George Ernest Cramer Ⓢ Sharpsburg, Pa.; University of Pittsburgh School of Medicine, 1913; aged 56; died, June 14.

Andrew J. Learned, Millfield, Ohio; Columbus Medical College, 1877; Civil War veteran; aged 97; died, June 22.

Robert Rolan Preston, Glade Spring, Va.; Medical College of Virginia, Richmond, 1904; aged 61; died, May 2.

William Henry Deardorff, Philadelphia; Jefferson Medical College of Philadelphia, 1896; aged 72; died, June 20.

William F. Golling, Springfield, Ohio; Homeopathic Hospital College, Cleveland, 1887; aged 79; died, June 29.

Joseph William Field, Owensboro, Ky.; Kentucky School of Medicine, Louisville, 1901; aged 60; died, June 16.

Charles F. Sullivan, Ardmore, Okla.; Medical College of Alabama, Mobile, 1890; aged 76; died, June 6.

Napoleon T. Langlois, Wyandotte, Mich.; Detroit College of Medicine, 1891; aged 71; died, June 15.

Harold Canter, Philadelphia; Jefferson Medical College of Philadelphia, 1938; aged 26; died, June 9.

Thomas R. Evans, Seattle; Louisville (Ky.) Medical College, 1906; aged 65; died, June 19.

Correspondence

ABOLITION OF THE RETENTION CATHETER

To the Editor:—In the June 15 issue of *THE JOURNAL* appears an article by Dr. Richard P. Middleton entitled "A Plea for the Abolition of the Retention Catheter in the Preparation of Patients for Prostatic Surgery." While there can be little disagreement with most of the author's statements and he is to be congratulated on a satisfactory solution to a vexing problem, it seems hardly fair to consign this potentially valuable procedure to desuetude without first raising a voice in its defense. The picture that he draws—"the more or less tender urethra with crusted mucopurulent exudate clinging to the tape which fastens the catheter to the penis, and not infrequent copious oozing of pus around the catheter"—is unfortunately all too common, and it must be admitted that some method of improving such a situation is desirable.

That improvement demands complete discarding of the retention catheter in favor of intermittent catheterization does not necessarily follow. Attention to a few simple principles will eliminate the undesirable by-effects of the procedure which has obvious and well recognized advantages. Particularly is it advisable to call attention to these principles in view of the facts that even the author admits the necessity of the post-operative use of the retention catheter, that occasional cases requiring catheterization with the help of a rigid stylet do exist and that the services of a well trained orderly are not universally available.

The first of these principles is reasonable attention to surgical cleanliness. The patient should be prepared as for a surgical operation, the preparation including shaving the suprapubic, scrotal and perineal regions and thorough washing of the entire area with soap and water. Drainage tubes and the receptacle should be sterilized, the latter when full, being replaced by another previously sterilized rather than taken out, emptied and returned. If irrigations are necessary, and these should be carried out preoperatively only in badly infected cases, a closed irrigation system consisting of sterile reservoir, glass Y tube and drainage tube will eliminate the introduction of organisms which is almost inevitable if the hand syringe is used and the drainage tube disconnected for purposes of irrigation.

The second consideration has to do with the size of the catheter. The fallacy that a large catheter is necessary for adequate drainage has been responsible for many cases of urethritis, prostatitis and periurethral abscess. When it is considered that a No. 5 ureteral catheter working somewhat less than half time in accord with the peristaltic action of the kidney pelvis can provide ample drainage for the urinary output of one kidney, it seems obvious that the lumen of a soft rubber catheter as small as a No. 12 French will furnish satisfactory drainage of the bladder even with the large fluid intake desirable for prostatic patients. Fully as important as drainage of the bladder is provision for the exit of mucous secretions of the urethra. A large catheter occupying the full lumen of the meatus, which is the narrowest portion of the urethra, causes retention of these secretions, favoring bacterial growth and often resulting in purulent urethritis.

The third point is the elimination of adhesive strapping by the use of a Foley type catheter. A few years ago at my request C. R. Bard Company started the manufacture of a No. 16 catheter of this type. This size represented a compromise between my desire for one of smaller circumference and the technical difficulties of production. Experience has proved that it is small enough to allow proper drainage of the urethra in most cases. In cases in which there is reasonably good kidney

function small doses of sulfanilamide, 15-20 grains a day (1 to 1.3 Gm.), provide added protection against infection.

The application of the foregoing measures have largely eliminated infection and urethral irritation, which appear to be the principal objections raised by Dr. Middleton to constant drainage. I agree entirely with him as to the advisability of operating in certain cases of prostatic obstruction without preliminary drainage, that infection should be avoided if possible and that "vaccination" of the urethra should be considered in the same category as "laudable pus." It has been my experience that all this can be accomplished by the proper use of the indwelling catheter.

Finally, I am not convinced that "being tethered to a bottle" is entirely a disadvantage. One of my patients was told by his son that what he needed to improve his health was a hobby, to which the old gentleman replied "Son, I have a hobby—keeping my water going." Possibly the responsibility of attending to his drainage apparatus may constitute one of the diversions which are as necessary to the well-being of the elderly patient as is physical activity. SAMUEL N. VOSE, M.D., Boston.

EFFECTS OF VACCINATION ON WASSERMANN TESTS

To the Editor:—In the *Illinois Medical Journal* for January 1940, Dr. R. D. Barnard reports the case of a blood donor who after many successively negative serologic examinations suddenly became Wassermann positive. It was suggested that the change in reaction was due to the presence of vaccinia. Since vaccination and serologic testing is a routine procedure at this institution, it was an easy matter to make a statistical examination of this fact. One hundred patients (fifty male and fifty female) with known recent negative serologic reactions were vaccinated and the blood Kahn tests repeated at intervals varying between twenty-nine and seventy-six days from the onset of the vaccination take. In no instance was a positive Kahn reaction obtained. We conclude from this that if vaccinia produces a positive blood Kahn reaction it does so in less than 1 per cent of cases and that therefore patients with vaccinia and a positive serologic reaction still require intensive investigation to eliminate other possible causes of the positive result.

ALFRED PAUL BAY, M.D.

MANNING I. SANKSTONE, M.D.

Chicago State Hospital, Chicago.

ASPHYXIA OF THE NEWBORN

To the Editor:—Permit me to call your attention to an omission in the special article on Pediatric Emergencies by Dr. Joseph Brennemann, published in the March 16 issue of *THE JOURNAL*, page 956. Asphyxia of the newborn is discussed without mention of the possible occurrence of congenital atresia of the postnasal orifices as a cause. Such "complete bilateral occlusion can cause alarming asphyxia in the newborn. The instinct for nasal breathing in the newborn is so impelling that, unless the mouth is forced open or the choanal occlusion is immediately broken through, asphyxia may result. It is the opinion of many writers (Lebensohn, J. E.: *Congenital Atresia of Postnasal Orifices*, *Ann. Otol., Rhin. & Laryng.* 32:1128 [Dec.] 1923. Cavanaugh, in discussion on Lebensohn. Clarke, J. P.: *Complete Congenital Occlusion of the Posterior Nares*, *Boston M. & S. J.* 138:171 [Feb. 24] 1898. Richardson, C. W.: *Congenital Osseous Obstruction of the Postnasal Orifices*, *Ann. Otol., Rhin. & Laryng.* 22:488 [June] 1913. Ronaldson, T. R.: *Note on a Case of Congenital Closure of the Posterior Nares*, *Edinburgh M. J.* 26:1035, 1880-1881) that surely a number of deaths listed as 'asphyxia neonatorum' have been caused by unrecognized, complete, bilateral choanal occlusion" (Morgen-

stern, D. J.: Congenital Atresia of the Postnasal Orifices, *Arch. Otolaryng.* 31:653 [April] 1940).

"In the newborn or in young infants, palpating with a probe or attempting to blow air through either nostril with a rubber bulb will help make the correct diagnosis. When the occlusion is membranous, rupture with a probe and dilation with the back of a small mastoid curet may give a satisfactory result" (Lemere, H. B.: Persistent Bucco-nasal Membrane in the Newborn, *THE JOURNAL*, July 31, 1937, p. 347).

It is important to emphasize to the obstetrician, pediatrician and general practitioner the fact that posterior congenital atresia exists and may be the cause of asphyxia in the newborn, requiring immediate relief.

DAVID J. MORGENSTERN, M.D., Brooklyn.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TONSILLECTOMIES IN DIONNE QUINTUPLETS

To the Editor:—Would you comment on the widely publicized wholesale tonsillectomies recently performed on the Dionne quintuplets? Those of us who try to protect the public from needless operations find it difficult to explain why such perfectly reared children should all at the same time have tonsils so diseased that they had to be removed. M.D., New York.

[Because of the great interest of this inquiry it was referred to Dr. Allan R. Dafoe, who replied:]

ANSWER.—There appears to be an implied suggestion in the inquiry to the effect that the removal of the quintuplets' tonsils was an example of unjustified "wholesale" tonsillectomy.

First of all let me make clear that I am opposed to the removal of tonsils when it is not necessary. In the case of the Dionne quintuplets the children had been subject to recurring attacks of tonsillitis of growing severity over the course of between two and three years.

Probably the best method of justifying these operations is to quote from successive reports of Dr. Allan Brown, physician in chief, Hospital for Sick Children, Toronto, professor of diseases of children, University of Toronto Faculty of Medicine. Dr. Brown is one of the foremost pediatricians of Canada and in my position as medical guardian of the Dionne quintuplets I have from time to time had the benefit of Dr. Brown's consultations.

On Nov. 6, 1938, Dr. Brown examined the children and reported: "In general their health is excellent with the exception of their tonsils and adenoids, which are in a chronic state of inflammation, which already accounts for the enlargement of their cervical glands—this latter is palpable evidence that the infection from their tonsils is spreading and at any time may get into the whole system, producing disastrous results such as an involvement of the heart or joints or even severe generalized infection with death.

"It would be difficult for any one to assume further responsibility for these babies unless their tonsils and adenoids were removed at once. This procedure should be done on all five at once and should not be attended with risk under the able guidance of Dr. Dafoe."

After this report, it would have been criminal for me to delay further. The operations were performed on November 9. Dr. Brown was present and examined the tonsils and adenoids as they were removed. I quote from his report:

Marie: "Tonsils rub against one another in midline. They are fibrous, chronically inflamed and ulcerated in deep fissures. Each tonsil is firmly adherent to walls of fossa. . . . Large, flat, mushy adenoid tissue was removed. . . . large post-nasal space. . . ."

Annette: "Tonsils very large, pink, no deep fissures. Ulcerated in various areas. Areas of fibrosis and ulceration with hemorrhage were seen when the tonsils were removed. Each tonsil firmly adherent to walls of fossa. Large flat adenoid tissue, one third the size of the larger tonsil was removed. . . ."

Emelie: "Areas of fibrosis and chronic inflammation. About twenty points of chronic inflammation on these tonsils. Large and distended. Each tonsil firmly adherent to the walls of fossa. . . . Spherical, very large, ulcerated adenoid pad."

Cecile: "Tonsils nearly touch. Most of surface ulcerated. Soft, pulpy and some fibrosis. Some crypts filled. Each tonsil firmly adherent to walls of fossa. Large fibrous adenoid. . . ."

Yvonne: "Tonsils nearly touch in midline. All the tonsil surface ulcerated. Tonsils one half the size of others but relatively large for her throat. Each tonsil firmly adherent to walls of fossa. Central form large mass of adenoid."

As a conclusion to this series of reports I quote from a report made when Dr. Brown visited the children on June 10, 1939, eight months after the operations: "It is a great source of satisfaction to see the remarkable improvement since the removal of their sources of infection. Their cervical glands (neck) are now normal and there is no sign of any deleterious effect that the diseased tonsils might have had. The operations will act as an insurance policy for their future health. . . ."

"As a result of this examination today I am able to say that it has amply justified Dr. Dafoe's decision to have their tonsils and adenoids removed last year. . . ."

I believe the foregoing series of reports constitutes an ample reply to the correspondent's suggestion.

As for the surprise expressed at the infection appearing in all five at the same time, I find that difficult to understand. I, on the contrary, would have been surprised if the infection had occurred only in part of the set. This is an identical set living in an identical environment. The appearance of a disorder in one individual and its failure to appear in others when no differences of heredity or environment exist would be surprising indeed to me.

As for the appearance of diseased tonsils in these children, I have no excuses to offer. It is well known that diseased tonsils occur in children of the best homes as well as those of the worst. We believe the care that has been given to these children is the best possible care we could have given them. These children are subject to outside sources of infection a great deal more than the public realizes, despite our attempts to protect them.

MYASTHENIA GRAVIS

To the Editor:—A patient with myasthenia gravis of three years' standing has been taking prostigmine, ephedrine sulfate and glycolixir with but temporary improvement. His case has followed the typical course of this disease. His present condition is so distressing that I hope you can suggest some additional help. Jesse Shoup, M.D., Washington, D. C.

ANSWER.—There is no "typical course" for myasthenia gravis. The disease progresses by remissions and relapses. The remissions may last for days, weeks, months or even years and the relapses for an equal length of time. Even when patients are at their worst, if they can be supported by large doses of prostigmine hydrobromide they may make an excellent recovery. Patients unable to chew, swallow, talk or lift their arms or legs or even their heads from the bed have recovered after weeks of illness. A few patients, moreover, have been carried through a difficult period of dyspnea by use of the Drinker respirator. If dysphagia is severe, prostigmine hydrobromide may be given by injection, and it is common with patients ordinarily taking prostigmine hydrobromide by mouth to use, on occasion, parenteral therapy. A nasal tube may be inserted when there is difficulty in swallowing, but this must be done with great care so that the tube does not, by mistake, pass into the larynx. Rectal feeding, or even intravenous medication with dextrose, is desirable. Every effort should be made to keep the patient normal both mentally and physically, for there is always a strong probability that, should he be carried through a severe attack, he will make a good and perhaps even a remarkable recovery. Prostigmine hydrobromide is by far the most dependable drug. It should be used in doses as high as from ten to fifteen 15 mg. tablets a day, or even more. Ephedrine sulfate is of some value in augmenting the effect of prostigmine hydrobromide. It should be given in doses of three-eighths grain (0.024 Gm.) three times a day.

The query does not give enough information on which to base any judgment with regard to the prognosis in this case. Although it states that the patient has been sick for three years, there is no indication as to whether the patient has had remissions and relapses, what muscles are involved, whether or not he has responded to prostigmine in large doses, and it does not state the doses that have been used. All these data would be necessary before a competent consultative opinion could be given. One would desire, moreover, to know the age of the patient. Viets and Schwab (*The Diagnosis and Treatment of Myasthenia*

Gravis, with Special Reference to the Use of Prostigmine, *THE JOURNAL*, Aug. 12, 1939, p. 559), in a study of forty-four patients observed by them over a number of years, lost four patients out of eighteen who were over 50 years of age but only one patient out of twenty-six under 50 years of age. Two of the patients in the older group who died failed to take prostigmine hydrobromide consistently. The most serious type of the disease, and the one that is usually fatal in spite of treatment, occurs in women from 18 to 25 years of age. In three cases of this type the response to prostigmine hydrobromide was never good, although large doses were used. The older patients, however, respond unusually well to this drug, and even when the patient is seriously ill the prognosis with regard to life is good.

MUSCULAR EXERTION

To the Editor:—I have noted varying statements as to the effects of weight lifting on the human body. Would you please give me an opinion as to the possible harmful, as well as beneficial, effects which might result from (1) exercises using light weights a number at repetitions of which would be for below the limit of exertion or strain, i. e. exercises which result in general and increased muscular tonus, growth and strength, and (2) heavy, limit weight lifting which involves "supreme effort" types of exertion with previous training and with or without a warm-up. It would be of added interest to have your opinion on the effects after long periods of such lifting.

Jack DeMent, Portland, Ore.

ANSWER.—There is no unequivocal evidence as to either the immediate or the delayed effects of various forms of weight lifting. Perhaps the nearest approach to an answer is found in Dublin's report (*Harper's Monthly Magazine*, July 1928) that most college athletes have a greater life expectation than other men of their age group. The exceptions included some of the older athletes (who had had little or no medical supervision) and crew men. These last have a task that approximates "limit weight lifting." In this connection it is worth noting that farmers have a smaller life expectation than many other groups and that Protestant ministers have a notably great longevity.

An important consideration is the age of the person in question. It is doubtful whether any form of weight lifting harms the well trained young man who is in good health, and even more doubtful that a "supreme effort" type of exertion is wise for most people after the third decade. As to the question of beneficial effects, it seems that the important considerations are, first, Do the exercises bring pleasure to the participant? and, second, Do the exercises impart grace and a sense of well-being? Solomon (Proverbs 20:29) has given good general advice:

The glory of young men is their strength;
And the beauty of old men is the gray beard.

POSSIBLE MERCURY HAZARD FROM MERCURY CLUTCH

To the Editor:—What is the possibility of mercury poisoning in an operator of a machine using a mercury clutch? This clutch is filled with mercury, which whirls around at great speed in the housing of the clutch. The housing is completely closed except for the opening of the tightly fitting shaft and two small openings which are closed by screw caps. The engineers who manufacture this clutch state that the loss of liquid mercury is negligible over a year's time and give as an estimate two or three drops in two years' time. There are from 3 to 6 ounces of mercury in each clutch. The heat generated is 270 F. During operation the operator has little or no need to handle this instrument. The question of poisoning was raised and although I thought that there was no danger I decided to ask your opinion.

M.D., Ohio.

ANSWER.—If, in fact, the total leakage of mercury is limited to "two or three drops in two years' time," no apprehension as to mercury poisoning need be entertained. Owing to the wearing of parts, it becomes an obvious possibility that in the course of time more leakage of mercury might arise than contemplated by the producing engineers. Metallic mercury sublimates at room temperature, which fact is of significance. At a temperature of 270 F. sublimation naturally would be much more active. However, so far as known, a temperature of 270 F. within the clutch housing would not lead to the building up of a pressure of mercury vapors such as would tend to force any mercury out around the shaft in the absence of erosion. The nature of this machine is not disclosed in the query, but, if stationary, leakage would be observable. Any considerable leakage such as a daily drop should occasion concern. A selenium test paper is available which, in the presence of mercury vapors in the atmosphere, changes color. Such a test should be made from time to time. If evidence of seepage is thus provided, an exposure should be regarded as existing. From an engineering point of view it is possible to construct mechanical devices of this character without any leakage and therefore without prospective dangers of mercury poisoning.

SERUM OR PLASMA FOR TRANSFUSION

To the Editor:—In view of the desirability of plasma transfusion as an emergency measure in the treatment of shock, is there any method of rapid coagulation or separation of plasma aside from centrifuging the specimen? What method would be the most rapid and satisfactory to obtain a clear plasma for transfusion when a centrifuge is not available and where banked blood or plasma is out of the question?

M.D., Idaho.

ANSWER.—Natural clotting of normal blood is relatively rapid (from two to ten minutes). Retraction of the clot is a slow process. Clotting of blood may be hastened by a variety of methods: whipping with glass rods, the addition of tissue extracts (thromboplastin, coagulins, thrombokinase) and the addition of foreign bodies such as glass beads. None of these methods are desirable, however, in the production of serum, and although coagulation is more rapid, the resultant clotted blood still requires centrifugation.

The collection of blood into an anticoagulant such as sodium citrate allows for the separation of plasma. Rapid separation of cells from plasma in unclotted blood also requires centrifugation. Otherwise several hours must elapse for natural settling of the cells.

Obviously, in the absence of a centrifuge, emergency plasma or serum preparation is not feasible. In view of the fact that serum or plasma may be stored for months if properly prepared in sterile containers, the logical solution to the problem would be to prepare serum or plasma in advance and to store it until needed, when it can be administered without any delay.

ACHING AND ITCHING HEELS

To the Editor:—A man aged 45, Jewish, a salesman, has had itching and a dull ache in the heels of both feet for the past four years. These symptoms are continuously present but do not usually interfere with his sleep. At times, however, he has awakened from sleep because of itching in both heels. Immersing his feet in warm water has given relief. At different times various sorts of heel pads, arch supports and elastic stockings have been tried with only temporary improvement. The past medical history has been essentially negative except for an episode of lumbar pain about seven years ago, at which time the patient wore a specially made brace and slept on a board. The back does not cause him any pain at present. The tonsils were removed at that time because they were suspected of being a focus of infection. The family history is negative. The patient smokes about twenty cigarettes daily. Physical examination was essentially negative. The weight was 150 pounds (68 Kg.), height 5 feet 9 inches (175 cm.). There was considerable dental repair. The blood pressure was 106 systolic, 74 diastolic. The heart, lungs and abdomen were normal. There were no significant orthopedic or neurologic observations. Peripheral vascular examination revealed the presence of dorsalis pedis and posterior pulses in both feet. This was confirmed by a normal oscillometric reading in both ankles. There were no abnormal color changes in the elevated and dependent positions. The temperature of the feet was not abnormal. Histamine tests revealed a normal circulation in the skin at each ankle, calf and thigh. X-ray examination of the heels was negative. X-ray examination of the entire spine and pelvis showed hypertrophic arthritic changes in the third, fourth, fifth, sixth and seventh cervical vertebrae. The thoracic spine was normal. Complete blood, urinalysis and blood Wassermann tests revealed no abnormalities. A spinal puncture revealed normal dynamics and normal microscopic and protein content. The spinal Wassermann and colloidal gold tests were negative. A paravertebral procaine block was performed on the right side. Three cc. of 1 per cent procaine hydrochloride was injected alongside the bodies of the second, third and fourth lumbar vertebrae. This injection resulted in a prompt rise in the skin temperature and increase of oscillation, which gave evidence of complete sympathetic paralysis. In spite of this anesthesia the pain in the heel was not relieved. Vitamin B₁ was given in 20 mg. doses intravenously daily for two weeks without result. The patient then stopped smoking abruptly with complete alleviation of the foot symptoms but he then had a constricting sense of pressure in the throat, not relieved by sedation or antispasmodics. He ascribed the throat symptoms to the cessation of smoking and after about four weeks he resumed his smoking habit. The result was that the sense of pressure in the throat disappeared in a few days and the foot symptoms reappeared in a few days and gradually regained their former intensity. Several months later he again experienced relief of foot symptoms when he ceased smoking and as before the throat symptoms developed so that he again resumed smoking. The result was that the throat symptoms disappeared and the itching and pain of the heels reappeared. What additional procedures or studies do you advise? Are such pressure symptoms in the throat known to occur when a habitual smoker stops smoking abruptly and completely? Would it be advisable to narcotize the peripheral nerves of the legs?

M.D., Pennsylvania.

ANSWER.—It is improbable that the situation described indicates organic disease, for thorough investigation has failed to demonstrate evidence of organic disease and there are signs of nervous instability. No reason is known why cessation of smoking caused disappearance of the distress in the heels unless this distress was psychogenic in origin. The occurrence of the constricting sensation or pressure in the throat on cessation of smoking is almost certainly psychogenic. It is suggested that the situation presented be surveyed thoroughly from the standpoint of a functional disturbance rather than from the standpoint of an organic disease.

AMBULATORY AUTOMATISM OR FUGUE

To the Editor:—I am 62 years old, 6 feet (183 cm.) tall, weigh 212 pounds (96 Kg.) and never had any serious sickness. I had influenza twice, both attacks mild, and was in bed about two days each time. I have never tasted alcoholic liquors of any kind and have been moderate in all my habits. I have just had a general physical check-up; the head and chest were roentgenographed, the Wassermann test was made, the urine, reflexes and eyes were checked, all with negative results. The blood pressure was 140 systolic, 90 diastolic. The heart was normal except that the aorta looked a little large. My complaint is this: About twenty years ago I was going on a night call when suddenly I appeared to be going in the opposite direction. Through reasoning I found the patient's home, examined him and treated him and got almost back to town when I suddenly became normal again. Then only a few nights after that I was returning from a country call and had it happen again. This time it was more persistent. I could not right myself after getting to town so stopped at my office and saw several patients who were waiting, yet all the time my directions were reversed. My office seemed on the wrong side of the street and the rooms in my office seemed in reverse order. I was afraid to try to go home alone as all the houses seemed to be on the reverse side of the streets, but on going into my house I instantly righted myself. There is no dizziness, no headache or nausea and my mind is perfectly clear except in orientation. Since then every time I come in my office at night the moment I enter my directions have become reversed and they stay that way until I go home, when I am suddenly righted. I never have had any indication of the trouble in the daytime. I have been examined by several good men but none ever heard of just such a case. It appeared to all that my center for orientation has gone haywire, but why or what caused it or how to combat it or what the outcome will be no one seems to know. I should like your opinion on diagnosis, prognosis and treatment and references if there are any.

M.D., New York.

ANSWER.—From the evidence submitted it appears that this is what is known as an ambulatory automatism. This is also known as a fugue or a psychic equivalent. This condition is related to epilepsy and occurs usually in place of the convulsion. There may be a complete amnesia for the attack or there may be complete retention of all facts during the attack. The attacks may last for minutes, hours or days. Usually when the attack lasts longer than minutes or an hour or two one must think of a hysterical reaction. From the history there is a loss of orientation in the attack. It is suggested that a physician administer sodium bromide 1 Gm. three times daily and increase the dosage gradually if and when the attacks do not cease. Have there ever been convulsions or loss of consciousness as a child or as a young adult? If the correspondent is unable to take bromides he can use phenobarbital in doses of 0.1 Gm. two or three times daily. The following books may be consulted:

Oppenheimer, Hermann: Text-Book of Nervous Diseases for Physicians and Students, Edinburgh, Otto Schulze & Co.

Jelliffe, S. E., and White, W. A.: Diseases of the Nervous System, ed. 6, Philadelphia, Lea & Febiger, 1935.

Dercum, F. X.: A Clinical Manual of Mental Diseases, ed. 2, Philadelphia, W. B. Saunders Company, 1917.

There is apparently no objective evidence of organic disease of the central nervous system in this instance. Lesions in the occipital and temporal lobes may cause auras or sensations such as described.

DISINTEGRATION OF WOOL DIAPERS

To the Editor:—Several mothers do not use rubber pants over the diapers of their infants. Instead they prefer a knitted wool pantalet. In one particular case the wool rapidly disintegrates and the structure falls apart. The baby is taking minute doses of iodine and is also taking cod liver oil, purified vitamin D in propylene glycol and ferrated maltine. These same substances are being taken by other babies, whose mothers are not experiencing the same trouble. The diapers in this case have been treated with mercury bichloride without any effect on the degeneration of the wool. Can you inform me what agent is acting to cause this process to continue?

M.D., Minnesota.

ANSWER.—As in this particular case the wool of the diaper disintegrates and falls apart, whereas it does not do this with other infants using the same type of diaper and taking the same medications, there are only about two possible explanations. (It is presumed that the diaper is of the same manufacture as those being used by the other infants. If not it might be wise to obtain diapers of the same manufacture because there is considerable variation in the price of diapers and their quality even in the same style of diaper or pantalet.) Either some agent is used in the washing of the diaper different from those used for the others or there is some peculiar chemical in the child's urine causing the disintegration of the wool (a high content of ammonia might conceivably cause trouble). If this baby's diaper after the urine has remained in it for some time smells strongly of ammonia, then this should be controlled in one or all of the following ways: by rinsing the diaper last in saturated boric acid solution; cutting down the fats in the baby's diet, or adding

one-fourth teaspoon of baking soda to each bottle of the formula for a week or so. Free ammonia is not present in the urine when first passed, and it is possible that soaking the diapers in water immediately after being wet might dilute the ammonium salts sufficiently before ammonia forms in considerable amounts.

BLEEDING FROM GUMS

To the Editor:—A white woman aged 53 complains of bleeding from the gums, especially in the morning before brushing her teeth. She has had this condition for the last fifteen years intermittently, and in spite of taking large amounts of fruit juices, ascorbic acid and calcium recently there has been no improvement. The gums are in perfect condition as confirmed by her dentist, and no lesions are apparent in the mouth. She does not bruise easily nor do any purpuric spots appear spontaneously. Her blood pressure is 170 systolic, 120 diastolic. The urine is completely normal. The red count is 4,310,000; hemoglobin content 72 per cent. The white count is 8,950, polymorphonuclear leukocytes 52 per cent and lymphocytes 48 per cent. The coagulation time is seven minutes. The platelet count is 408,000.

Alvin A. Rosenberg, M.D., Morristown, N. J.

ANSWER.—Without more detailed information the question can be answered only by assuming what might be the relationship between the physical conditions mentioned and the oral condition, since the statement is made that "the gums are in perfect condition." Presumably the bleeding is nothing more than capillary oozing which causes the saliva to be blood tinged. Since the bleeding has been intermittent, it is possible that the condition is associated with the menstrual periods, if still existent. This question should be carefully checked. The literature contains reports of sex hormones being associated with gingival disorders. Although it is impossible to make definite statements regarding the relationship of the complaint to the blood picture, some obscure hemorrhagic diathesis on which is superimposed a low grade chronic inflammation of a septal gingiva in a posterior segment of the dental arch can be considered. Lastly, one would suggest consideration of the entire group of vitamins, more especially A, B and K. It might be of value to determine the ascorbic acid level of the fasting blood plasma on the basis that the patient was not capable of utilizing all the ascorbic acid taken in the diet or administered as a supplement.

REFRACTORY PRURITUS VULVAE AND ANI

To the Editor:—A woman more than 70 years of age has been suffering from pruritus vulvae and ani for the last five years. The pruritus is combined with a senile vaginitis, kraurosis and leukoplakia of the tongue. In the night time especially the itching is bad and sedatives such as the bromides and barbiturates often aggravate the itching. In the last few months the itching developed on her feet and there was a burning sensation of the tongue. There is oftentimes an itching around the lips. All laboratory examinations, including blood sugar, blood calcium, vaginal smear and stool, showed negative results. There was a moderately increased blood sedimentation rate. Local treatment consisting of high voltage x-rays, ultraviolet rays, alcoholic injections, estrogenic injections, and estrogenic hormones in vaginal suppositories, polyglandular injections, thyroid tablets, vitamin B₁ hydrochloride, later vitamin B complex, nicotinic acid, alkalinizing of the system, calcium, various tonics and vaginal infiltration of 3 per cent tannic acid in glycerin, kaolin ointments, insulin injections and a purine-poor diet did not give any improvement. The patient is excitable, nervous and unable to sleep. She admits that the nervousness aggravates her condition and if she is occupied the itching subsides a little. The nicotinic acid injections, 50 mg. given every other day, altogether six injections, gave her an urticaria-like reaction. She does not want to continue because she did not see much progress. Kindly advise me what kind of treatment would come into consideration. What kind of sedatives, if any, in injection form would be advisable? Would continuance of the nicotinic acid (perhaps in highest doses of 100 mg.) be advisable? Kindly explain what the urticarial reaction is due to.

M.D., New York.

ANSWER.—The patient has had almost the entire gamut of therapeutic measures generally used to treat pruritus vulvae and ani and other forms of pruritus. Perhaps, however, none of these substances have been given a thorough enough trial. What the patient most likely needs is a combination of a sedative, local soothing applications and estrogen therapy. Any one of the mild sedatives which does not produce disagreeable symptoms should be prescribed for a number of days at a time. Perhaps small doses of chloral hydrate or barbiturates may be tolerated by the patient. There is no need to administer the sedatives by injection. Furthermore internal estrogenic therapy may be given for a brief period. Long continued administration of estrogenic substance should be discouraged, and careful inquiry should be made of the family history. Temporary relief may be obtained by using cold compresses locally. In some cases heat helps but in others it aggravates the itching. The application of pure honey has given relief to some women. A lotion or salve containing phenol or sodium thiosulfate may also be helpful temporarily while waiting for the estrogens to take effect.

The patient should be advised to avoid rubbing the involved parts when cleansing the anus and vulva after a bowel movement or urination. The parts should be patted and not rubbed and it is best to use soft cotton or soft tissue rather than ordinary toilet paper. Scratching aggravates the condition; hence the patient should be advised to pinch the part which itches or, better still, make firm continuous pressure on the part with the closed fist or a few fingers. Since the nicotinic acid gave the patient an urticaria-like reaction which added more areas of itching, this medication had better not be repeated.

Suggestive therapy in the form of informal psychotherapy may be helpful.

GROWTH OF LONG BONES

To the Editor:—What would be the proper management of the following case? A 7 year old boy whose birth date is November 1932 was injured in an automobile accident in June 1937. A compound fracture of the left tibia in the region of the ankle resulted. Osteomyelitis at the site of the fracture developed about four weeks after the accident. The leg brace was removed one year ago. X-ray examination shows complete loss of growth at the lower tibial epiphysis. The left tibia is three fourths of an inch shorter than the right. The left foot is slightly "turned in" at the ankle as a result of the continued growth of the left fibula at both its epiphyses and the stoppage of growth at the left epiphysis of the left tibia. The boy apparently walks at a normal gait and runs and jumps without any pain. The leg has not drained for about one and a half years. The external malleolus of the left foot is slightly more prominent than the right external malleolus. The boy's parents and his brothers and sisters average about 5 feet 4 inches (162.5 cm.) in height. How much of the tibial longitudinal growth takes place at the upper epiphysis and how much at the lower epiphysis? What is the rate of growth of the tibia and fibula at the various ages from the time of birth to the time of normal complete ossification of its epiphyses? Approximately how much more growth (average) of the lower legs at the lower epiphyses can be expected until growth ceases? At what age do the two epiphyses of the tibia become fused? Would a brace be advisable to prevent any further deformity? Would a shoe with the outer portion of the sole and heel slightly thicker than the inner portions be advisable in an attempt to prevent further deformity? Would a resection of the left fibula including removal of the lower cartilage plate be advisable now or later? Would osteotomy for lengthening the tibia be advisable now so far as the tibia has been the site of a previous osteomyelitis? Should stoppage of growth of the lower epiphyses of the two bones of the sound lower leg be instituted at the time of resection of the left fibula and operative intervention to prevent further growth at its lower (left fibula) epiphysis? Should the scar at the site of the injury be removed? When? How far would "inversion" of the foot progress if left untreated? What complications would arise if the foot should be left unaltered until bony growth in the long bones of the leg ceased? The left ankle joint (intra-articular surfaces) is normal in every respect.

M.D., Michigan.

ANSWER.—Most of the growth in the lower extremity occurs in the region of the knee joint. Piersol gives the eighteenth and nineteenth years as the periods in which the lower epiphysis of the fibula unites and the eighteenth year for the ossification of the lower epiphysis of the tibia. Dr. Dallas Phemister, of the University of Chicago, has been a pioneer in this country in the arrest of the growth of the epiphysis to produce shortening in sound limbs. Reference to his writings will give much information. Each patient is an individual problem, and a definite answer such as this inquiry requires cannot be given.

SISAL FIBER, OR HEMP, AND ALLERGY

To the Editor:—Have you any information as to the allergic properties of sisal fiber as used in mattresses? Are there any known cases on record of sensitiveness to this product? To what group or family of plants is it related?

Francis J. Cenedella, M.D., Moline, Ill.

ANSWER.—A search of the literature has revealed no report as to the allergic properties of sisal fiber, or hemp (henquen), which is the product of the *Agave rigida* variety of *sisalana*. *Agave* is a member of the order *Amaryllidaceae*; the century plant, *Agave americana*, is the best known species of the genus. An inferior fiber is obtained from another species, *Agave decipiens*. The fiber is obtained from the leaves. In conjunction with manila or alone it is used extensively for cordage and binder twine. The plants grow extensively in Florida, the Bahamas, the West Indies, Yucatan and other parts of Central America.

According to a letter from Berlin (*THE JOURNAL*, Aug. 5, 1939, p. 522) Lehmannsick read a paper before the Medizinische Gesellschaft of Bonn in which he stated that during the course of an expedition to Tanganyika in 1938 he found that pneumoconiosis, sometimes followed by tuberculosis, occurred in native workers. In the preparation of sisal the native brushes hemp on brushing machines, forming great clouds of dust which consist of small hemp fibrils and earth dust from the plants and which cover the workers like layers of flour. It has been estimated that the worker in such shops can endure the work for seven or eight years at most.

LACQUER SPRAYS IN BEAUTY PARLORS

To the Editor:—I should like to know the active ingredients of the lacquer spray used in beauty parlors. Is there any reason to believe that a beauty operator using such a spray over a period of time would develop a peribronchial pulmonary fibrosis?

M.D., Wyoming.

ANSWER.—A variety of commercial hair lacquers are available to beauty parlors, every one different as to constituents and quantities of constituents employed. A typical formula for a heavy hair lacquer is:

Resin	15 parts
Sandarac	10 parts
Benzoin (Siam).....	20 parts
Alcohol (96%).....	50 parts
Perfume	5 parts

The possibility exists that operators may become sensitized to the resinous constituents of lacquers and may present manifestations of cutaneous disease, asthma, bronchitis and the like. In fact, cutaneous diseases among beauty parlor operators are fairly common, but since so many chemicals may be used it is difficult to determine the offending agent. It is not possible to state that a peribronchial pulmonary fibrosis is a characteristic result of exposure of any duration or severity to hair lacquers.

SALTPETER IN FOOD

To the Editor:—Recently I have received many inquiries from students and parents regarding the use of saltpeter in food in institutions, allegedly for the purpose of reducing sex interest. Some persons are so convinced that this is being done that they attribute menstrual disturbances, which frequently follow a change of environment, to this drug. I can find nothing in pharmacopoeias indicating that it has such a function, nor do I know that it or any other drug has been used in this way. Yet there are people who are positive that institutions employ it, and I should like to quell this rumor once and for all here.

M.D., Texas.

ANSWER.—Saltpeter is said to be used extensively in institutions and camps, but there are no published statements that could be quoted, and rumors are often based on queer tasting coffee, which may have other causes. The anaphrodisiac action, if any, is probably largely suggestive, but it is imaginable that the general depressant action of continued use of the drug might have such a result. No critical observations have been reported, nor is the effect discussed in modern books; but Stillé in his "Therapeutics and Materia Medica" (Philadelphia, Lea & Febiger, 1874, p. 613) states, under Potassium Nitrate, "In the last century, Alston described it as resolvent, antiseptic, antiphlogistic, diuretic, purgative and anaphrodisiac." Contrary to popular rumor, saltpeter is not valuable as an anaphrodisiac, and its use by cooks or other laymen in institutions cannot be too strongly condemned.

SENSITIVITY TO SERUM

To the Editor:—On a form for medical examination used by the Boy Scouts of America (collogue 4/26, form C-950) the following question is asked: "Do you think this boy is likely to be sensitive to serum inoculations?" In the absence of a suggestive history the only way I could give the desired information would be by use of cutaneous tests with serum. Please tell me something along this line that will help to judge individual sensitivity to serum? I have had some odd reactions with injections of serum in persons who apparently present nothing to indicate untoward reactions; hence as a routine I always have epinephrine at hand.

Frederick J. Simmonds, M.D., Boston.

ANSWER.—In the absence of a history of asthma or information concerning any allergic condition, it is not possible to judge that an individual is sensitive to serum unless appropriate tests are made. As the majority of serums are from the horse, it is likely that an individual sensitive to one specific serum would also be sensitive to most other serums.

FREQUENCY OF SCHICK TESTS AND REVACCINATION

To the Editor:—In doing school work I encounter considerable disagreement among the profession as to how often Schick tests should be given children who have previously had a negative test. Will you kindly inform me what the best opinion is? Another question on which there is disagreement is how often children should be revaccinated.

M.D., Indiana.

ANSWER.—If the Schick test is negative in an individual who has not been immunized artificially against diphtheria by the customary means, it should not be necessary to repeat the test on future occasions. However, when a negative Schick test has been secured as the result of immunizing inoculations, future Schick tests should be performed for the purpose of determining the duration of the immunity that was artificially established. The length of time artificially induced immunity endures depends on the antigenic material and the dosage used. Under some circumstances it would be well to perform a Schick test once a year whereas, if the best procedures for active immunization

are followed, the average immunity should last from three to five years or even longer. Then Schick tests could be repeated after such intervals of time have elapsed.

If a child was successfully vaccinated during the first year of life and revaccinated successfully when entering school, immunity, in most instances, would probably endure for life. Some health departments recommend that revaccination be performed every five years. Regardless of any past vaccinal history, every individual should be vaccinated immediately after any known exposure to smallpox. An individual with a typical vaccination scar seldom contracts smallpox.

ORDER OF IMMUNIZATION IN CHILDREN

To the Editor:—What routine procedure of immunization is indicated in a child, according to the best present day practice? At what ages and in what order should they be applied? How often should they be repeated?

M.D., Colorado

ANSWER.—It is well to perform vaccination against smallpox within the first three months after birth. Next in order, immunization against whooping cough is advocated by many. Ordinarily this procedure is not advised prior to the second half year of life. As a rule, when the child has reached 9 months of age it should be immunized against diphtheria. At this time the combined method of establishing immunity against both diphtheria and tetanus may be adopted. Between the ages of 1 and 2 years consideration may be given to inoculation of the child with streptococcus toxin for the purpose of establishing immunity against scarlet fever. Some hesitate to resort to the last named procedure because of the possibility of severe reactions. Vaccination against smallpox should be repeated when the child enters school and again before entering college. Schick and Dick tests should be done when school age is reached in order to determine whether further immunizing substances are required.

CONVALESCENT SERUMS FOR CONTAGIOUS DISEASES

To the Editor:—Please send me information on convalescent serum for measles, mumps, whooping cough and scarlet fever. Also please advise where they can be obtained.

H. E. Mohley, M.D., Morrilton, Ark.

ANSWER.—Human convalescent serum is of value for the prevention of measles and scarlet fever if given soon after exposure in doses of 5 to 10 cc., depending on the age of the patient. Meader of Detroit has reported good results with convalescent serum for the prevention of whooping cough. For mumps prophylaxis convalescent serum is adopted less frequently than for the other diseases mentioned. Human convalescent serum has been used for the treatment of each of these diseases but is undoubtedly of greatest value in scarlet fever.

In the Middle West there are the Milwaukee Serum Center and in Chicago the Samuel Deutsch Serum Center at Michael Reese Hospital. The Detroit Department of Health also maintains a center for the preparation of human convalescent serums.

Further information may be obtained from an article by A. L. Hoyne, "Immunologic Methods in Pediatrics" (THE JOURNAL, April 22, 1939, p. 1581), also from an article by Hoyne, Levinson and Thalhimer, "Convalescent Scarlet Fever Serum" (*ibid.*, Sept. 7, 1935, p. 783).

STAINED TEETH FROM FERROUS SULFATE

To the Editor:—What can be done to prevent staining of the teeth in anemic children when ferrous sulfate in powder form is administered?

Horry Wexler, M.D., Brooklyn.

ANSWER.—The discoloration of teeth from the use of ferrous sulfate in the treatment of anemia is superficial and does not penetrate the tooth substance. A thorough prophylaxis which removes the film deposited on the surface of the teeth will remove this stain. There should be little discoloration if the ferrous sulfate is given in tablet or capsule form or if it is prescribed in a heavy syrup.

COMPLICATIONS AND PROGNOSIS IN BURNS

To the Editor:—1. Please give me some information regarding the prognosis of a first degree burn that covers more than half the body. 2. Is nephritis the most common complication of burns over a large surface of the body?

J. O. McKenney, M.D., Beaver Dam, Ky.

ANSWER.—1. The prognosis of a first degree burn that covers more than half the body is good. This has been proved many times by individuals suffering from extensive sunburn.

2. The most common complication of burns over a large surface of the body is infection and toxemia. Nephritis would be considered a part of the complication of toxemia.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, August 3, page 406.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, Sept. 11-13, to be given in medical centers having five or more candidates desiring to take the examination. Part III, Baltimore and New York during October and Boston during November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written*. Various centers. Feb. 20. Final date for filing application is December 21. Orol. Cleveland, preceding A. M. A. convention. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written*. Various centers, Oct. 28. Applications must be on file not later than Sept. 16. Orol. Chicago, Dec. 6-7. Applications for Group A must be on file not later than Nov. 1. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. October 21. Applications must be on file not later than September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 18-19. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: Orol. Cleveland, Oct. 5. *Written*. Various centers, March 8. The only written examination during 1941. Applications must be on file not later than Dec. 1. A special oral and clinical examination will be held on the Pacific Coast during 1941 providing there will be enough candidates to warrant it. Applications for this examination should be on file not later than Sept. 15. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and written*. New Orleans, January 1941. Final date for filing application is November 15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: New York, March 30-31. Following the Region I meeting of the American Academy of Pediatrics, Chicago, May 18. Following the Region III meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Orol. New York, December 18-19. Final date for filing application is October 8. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Boston, Sept. 26-29. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written*. Part I. Various centers, October 21. Final date for filing application is September 15. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Oral and written*. Chicago, February 1941. Applications must be on file not later than Oct. 15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

New York Endorsement Report

Mr. Herbert J. Hamilton, chief, Bureau of Professional Examinations, reports fifty-one physicians licensed by endorsement from March 31 through June 29. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
College of Medical Evangelists.....	(1939)	N. B. M. Ex.
Colorado School of Medicine.....	(1902)	Colorado
University of Colorado School of Medicine.....	(1926)	Colorado
Georgetown University School of Medicine.....	(1938)	N. B. M. Ex.
Emory University School of Medicine.....	(1938)	N. B. M. Ex.
Northwestern University Medical School.....	(1939)	N. B. M. Ex.
Rush Medical College.....	(1937)	N. B. M. Ex.
The School of Medicine of the Division of the Biological Sciences.....	(1938)	N. B. M. Ex.
Indiana University School of Medicine.....	(1932)	Indiana
University of Kansas School of Medicine.....	(1932)	Puerto Rico
Johns Hopkins University School of Medicine.....	(1937)	Maryland
Boston University School of Medicine.....	(1936)	N. B. M. Ex.
Harvard Medical School.....	(1933)	N. B. M. Ex.
Tufts College Medical School.....	(1938)	N. B. M. Ex.
Wayne University College of Medicine.....	(1937)	N. B. M. Ex.
University of Minnesota Medical School.....	(1939)	Minnesota
St. Louis University School of Medicine.....	(1925)	Missouri
Washington University School of Medicine.....	(1938)	N. B. M. Ex.
Columbia University College of Physicians and Surgeons.....	(1933)	New Jersey, (1937), (1938)
Cornell Univ. Med. College (1935), (1936), (1937),	(1938)	N. B. M. Ex.
Long Island College of Medicine.....	(1938)	N. B. M. Ex.
New York Med. College and Flower Hospital (1936),	(1937)	N. B. M. Ex.
New York Medical College, Flower and Fifth Avenue Hospitals.....	(1938, 5)	N. B. M. Ex.
New York University College of Medicine.....	(1937, 2)	N. B. M. Ex.
University and Bellevue Hospital Medical College.....	(1935)	N. B. M. Ex.
Eclectic Medical College,	(1939, 2)	Ohio
Western Reserve University	(1935)	Ohio
University of Cincinnati	(1939)	N. B. M. Ex.
Jefferson Medical College of Philadelphia.....	(1938)	N. B. M. Ex.
Vanderbilt University School of Medicine.....	(1936)	N. B. M. Ex.
(1937) Tennessee		
University of Vermont College of Medicine.....	(1936)	N. B. M. Ex.
University of Virginia Department of Medicine.....	(1938)	Virginia

Medical School.....(1937) Wisconsin
Medicine.....(1937) N. B. M. Ex.
Medizinische Fakultät,
Regia Università degli Studi di Roma. Facoltà di
Medicina e Chirurgia.....(1937) New Jersey
Université de Genève Faculté de Médecine.....(1935) New Jersey

Book Notices

As I Remember Him: The Biography of R. S. By Hans Zinsser. Cloth. Price, \$2.75. Pp. 443. Boston: Little, Brown & Company, 1940.

Already widely celebrated by numerous reviews in literary publications, this volume by Dr. Hans Zinsser may be recommended as required reading for every young physician who wishes inspiration, and for every older physician who can appreciate the best in the field of medical literary contributions. It was selected by the Book of the Month Club as its choice for July.

Assuming a somewhat unusual technic, Dr. Zinsser discusses his own life as if it were that of a dear friend with whom he was intimate. The flavor of the book is that of soft reminiscence, modified by writing full of strength, modified by scientific historical records, modified by philosophic cogitation, all of which makes it extraordinary beyond any other personal memoirs that have become available. Comparison may be odious, but this autobiography stands high above any of the popular autobiographic contributions to medicine that have regaled the public during the past few years.

Here are first hand accounts of many of the scientific great and near great who have occupied the medical scene during the past four decades. Here are evaluations of psychoanalysis and the place of women in science and in life. Here is a defense of physicians' conservatism which deserves quotation:

To a moderate degree, then, conservatism is useful. But by far the more important causes of lag lie in the nature of the work which medicine is called upon to perform. The doctor's profession is, in part, an art, since it deals with matters that demand manual skill; in part, again, it is a branch of that vague middle ground between the physical and the psychological, in which emotional intelligence and great sanity of judgment are required; it is, like all biology, an application to an unlimited variety of problems of the reasoning and the techniques of all available science.

For every one recently interested in the discussions of socialized medical practice, this point of view deserves consideration:

At the present time, there is a strong popular movement for the socialization of medical practice, and an effort, essentially praiseworthy, to bring the benefits of discovery and of improved care within the reach of the population as a whole, irrespective of ability to pay. This is as it should be, and there is little question of the fact that the old system of charity clinics and hospitals no longer meets modern requirements. Moreover, it is morally sound to postulate that all discovered means of alleviating suffering and sorrow, maintaining health and preventing death, should be freely available to all that need them—without reference to social, racial, or economic condition. This will demand a complete reorganization of practice, in which the medical profession must, and should, play the leading role; and undoubtedly it will—though there has been a tendency on the part of reformers, sociologists, government agencies, and professors of the teachers' union type to assume that reluctance to accept any and all proposals indicates a conservatism of self preservation based on purely venal motives. Let it not be forgotten that the situation as it now exists is entirely the consequence of the progress made in medical discovery by the profession itself; that the enhanced power for good which is now claimed as the latest of the inalienable rights of man is the result of the labors of medical investigators and practitioners, and that public health organization, social service, group practice, and all other advances which have revolutionized the relationship of medical knowledge to the population—even housing, nutrition, and the sociological conditions that influence health, such as wage scales, public parks, industrial hygiene, etc., etc.—were given their basis of factual observation and their early organization for practical application by the insight of medical men.

There is in the practice of medicine a unique quality that is a source both of inspiration and of terror to the conscientious young physician. Dealing as it does with matters of life and death, any lack of knowledge or of skill becomes a positive fault of omission and even guilt. If a patient dies or is incapacitated—with all the heartbreak and suffering that this implies—because the attending practitioner was ignorant of measures that are available and that might have brought another outcome in more skilful hands, he is as responsible as though he had committed a wilful injury. This is true not only of surgical procedures, but equally—perhaps more frequently so—in infectious diseases, where speed and precision of diagnosis by well known methods and vigorous intelligent treatment may decide the issue within a few hours, one way or the other. It is this consideration, more than any other, which—with the growing accumulation of knowledge that no one man can hope to master

completely—has automatically led to the organization of group medicine, the increasing cooperation of city and state health departments, and the more generalized utilization of hospital facilities. And since it is essential that all effective knowledge must be applied to rich and poor alike, unless our profession is to lose the fine, ancient traditions of its history, a considerable readjustment of its activities is inevitable. These simple considerations are at the bottom of all the agitation for the so-called "socialization" of medicine on which great volumes of reports have already been issued. It should not be forgotten, however, by the ardent lay reformers that evolution in these directions has long been going on within the profession itself, and, within a single span of professional life, enormous progress—almost entirely originated by public spirited doctors—has been achieved. Controversies have turned not at all on the objectives to be attained, but rather upon the manner in which the reorganization is to be carried out.

There are discussions of euthanasia with examples which make exceedingly clear the author's point of view. There are brief excursions in obstetrics, and many physicians will appreciate, as the result of his own experiences, the humor and insight which the author has for this part of the physician's occupations. Then comes the time when Zinsser becomes a great public citizen. You travel with him to Serbia, to Russia, to Africa and to the Far East, to Mexico and to France. You come at last to his chapter on "Philosophical Confusion," which is farewell to the present and his forecast for the future. He describes his own death. Where in literature is there to be found a contemplation of dissolution like the following?

As his malady progressed, he had another variety of experience which, to some others more conditioned to religious belief than he was, might have signified an intimation of the separateness of body and soul.

He said to me: "Here I am, me as always. My mind more alive and vivid than ever before; my sensitiveness keener; my affections stronger. I seem for the first time to see the world in clear perspective; I love people more deeply and more comprehensively; I seem to be just beginning to learn my business and see my work in its proper relationship to science as a whole; I seem to myself to have entered into a period of stronger feelings and saner understanding. And yet here am I—essentially unchanged except for a sort of distillation into a more concentrated me—held in a damaged body which will extinguish me with it when it dies. If it were a horse I was riding that went lame or broke its neck, or a ship on which I was traveling that sprang a leak, I could transfer to another one and leave the old vehicle behind. As it is, my mind and my spirit, my thoughts and my love, all that I really am, is inseparably tied up with the failing capacities of these outworn organs.

"Yet," he continued, apostrophizing in a seriocomic mood, "poor viscera, I can hardly blame you! You have done your best, and have served me better than could be expected of organs so abused. When I think of the things that have flowed over and through you! Innumerable varieties of fermented hops and malt and of the grapes of all countries and climates: Vouvray, Anjou, Chablis, Haut Sauternes, Chambertin, Nuits-Saint-Georges, Riesling, Lachryma Christi, Johannissthaler, Berncastler, Saint-Julien, Clos de Mouche, Liebfrauenmilch; endless amounts of pinard and vin du pays; the sour wines of Alsace, of North Africa, and of the Pyrenees; the stronger ones of Spain—Oporto, Sherry, Madeira, Malaga; the Tokay of Hungary; sparkling vintages of Burgundy and of Champagne; Veuve Cliquot and her brothers Mumm and Pommery; and the California brews hought in demijohns; to say nothing of the distillates—flavored and unflavored; cognac, Three-Star Hennessy; whiskeys—Scotch, Irish, Canadian, rye, bourbon, and the yellowish moonshine, colored with chicken droppings, from the Blue Hills; and gin—genuine and synthetic; Schlibovitz from the Balkans, Starka from Poland, and the vodka of the Steppes; erème de menthe and cacao, Marie Brizard, Cointreau, and Calvados.

"No, no, my organs! I cannot feel that you have let me down. It is quite the other way round. Only now it seems so silly that you must take me with you when I am just beginning to get dry behind the ear."

Words fail to give any adequate picture of this exceptional book. Again the reviewer can only say that the physician who fails to read and to reread it again and again is depriving himself of some of the finest hours that literature can afford to a thoughtful man.

The Foot and Ankle: Their Injuries, Diseases, Deformities and Disabilities. By Philip Lewin, M.D., F.A.C.S., Associate Professor of Bone and Joint Surgery, Northwestern University Medical School, Chicago. Cloth. Price, \$9. Pp. 620, with 303 illustrations. Philadelphia: Lea & Febiger, 1940

Here is a book filled to overrunning with a great deal of valuable and interesting information concerning the foot and the ankle. The author's first paragraph in the preface gives the key to the book: "The purpose of this book is to guide the student, general practitioner, industrial surgeon and younger orthopedic surgeon in the diagnosis and treatment of diseases, deformities and disabilities of the foot and ankle. It presents in natural sequence and concise language the underlying principles of etiology, pathology, diagnosis and treatment of congenital, static, infectious, paralytic and other lesions. Traumatic lesions including fractures, dislocations and industrial conditions are

given special attention. I endeavored at the outset to describe and illustrate everything that could happen to a human foot and ankle, but I soon found that it would make two volumes or one that was unwieldy."

A foreword by Dr. Michael Hoke, wherein he pays tribute to Dr. Lewin's efforts, is further made interesting by a hope that someday he (Hoke) may present in book form the full exposition of his thoughts on the subject. The medical profession would welcome such a book.

In another foreword Dr. Morris Fishbein calls attention to the fact that there is a tendency, with specialization, to detract considerably from attention to the body as a whole and to consider various organs and portions as if they were independent. Dr. Lewin has evidently been aware of this tendency, because he quotes the late Dr. W. J. Mayo as follows: "One cannot divide the patient into parts for repair as he can an automobile but must treat him as a human being, and the treatment given must be the best that the combined knowledge of science can afford."

The book is written in readable form and not in what might be called the jargon of the specialist. There are many descriptions of various valuable tricks of the orthopedic surgeon that the practitioner can just as well use and the author expresses the hope that his book "will make the mysteries of the foot and ankle an open book to the general practitioner."

The book is "dedicated to the memory of Dr. Allen B. Kanavel." Dr. Lewin says that in 1915 Dr. Kanavel said to him "Lewin, I wish, some day, you would do for the foot what I have tried for many years to do for the hand." Hence the book.

Considering the field, and the thoroughness with which Dr. Lewin has tried to cover it, there is little of a critical nature that can be fairly uttered. The book is of convenient size, the paper is good, the print is easily read and the illustrations are numerous. A few errors in referring to illustrations are to be noted and there are some repetitions, but these are minor faults. It might be said that too many methods of treatment are given and that the author fails to evaluate them. However, on careful reading, the author's preference is usually to be found. Perhaps he should have emphasized his own views a little more strongly. Also frequent references are made to opinions of others on controversial questions but in many instances no footnote or reference in the bibliography can be found to direct the reader to the original article. A complete bibliography, however, would greatly have increased the editorial work and one can always go to the *Quarterly Cumulative Index Medicus* if one is really interested. All in all, the book is well worthy of a place not only in the library of the specialist but also in that of the practitioner. The author is to be congratulated on an effort that has been well carried through to a result that will serve a useful purpose.

Transactions of the American Philosophical Society Held at Philadelphia for Promoting Useful Knowledge. New Series—Volume XXXI, Part II: Chronic Arthritis in Wild Mammals. By Herbert Fox, Professor of Comparative Pathology, University of Pennsylvania, Philadelphia. Paper. Price, \$2. Pp. 73-149, with illustrations. Philadelphia, 1939.

Chronic arthritis stands high in the list of human ailments, and it incapacitates great numbers of people. Our knowledge of its nature and cause is lamentably inadequate. Studies in "comparative rheumatology," on how arthritis affects animals and whether such arthritis resembles the type which affects human beings might be supposed to throw some light on the problem. A few reports have been made on the disease as found in domestic animals but no reports have been made on its occurrence among wild animals.

Herein, Fox has reported results of an analysis of 1,749 skeletons and necropsies of animals. Some animals were captive specimens; many were wild animals killed in their natural environment. The material was from several institutions: the Philadelphia Zoological Garden; the Wistar Institute of Anatomy, Philadelphia; the National Museum, Washington; the Wagner Free Institute of Science, Philadelphia; Western Reserve University, Cleveland; the Academy of Natural Sciences, Philadelphia; the American Museum of Natural History, New York City. Among the great diversity of animals studied were seventy-seven whose skeletons showed definite

arthritic changes. The articular lesions of the captive animals and of the wild animals were entirely comparable. These lesions were common among certain varieties, for example Felidae, Hyenidae, Ursidae, Bovidae, Cervidae and especially anthropoid apes and baboons, rare or absent among certain Carnivora (Canidae) and among Rodentia (rats, mice, beavers, squirrels) and Chiroptera (bats).

Descriptions of the seventy-seven arthritic animals were given, based on studies of dried skeletons from museum or wet-cleaned bones at necropsy. These descriptions are amplified by more than sixty photographs of gross specimens and roentgenograms. The commonest lesion present was hypertrophic arthritis of the spine and was found in almost every case. Carnivorous animals exhibited "productive articular and periarticular disease" more often than did herbivorous animals; the latter more often presented "porotic and ulcerative articular lesions." Arthritis of extremities was noted in all varieties, but forelimbs were more affected in Carnivora, hind limbs in Artiodactyla. Contrary to the opinion of some that arthritis most often affects the most mobile portions of the spine (in human beings at least) Fox reported that in animals spondylitis occurs where the greatest stabilization of the spine is demanded for the animal's locomotion; that is, at the sites of greatest muscle rigidity or tonicity (sites of "osseomuscular fixation" or "stabilizing tension"). The presence of the arthritis was analyzed in relation to various other factors: the general body type, habits as to diet and "home life," age and associated morbid states. No relationship was found between the presence of the arthritis and zoogeography, ecology, individual habits, diet, associated diseases, and focal infection such as dental and alveolar disease. Finally, the author "cautiously suggested" that the hypertrophic or osteoarthritic lesions of these animals were strongly similar to those of osteoarthritis of human beings and that certain lesions seen especially in gorillas resembled rheumatoid arthritis of human beings.

The material seems to have been carefully studied and the results are concisely presented. Although the work would appeal more strongly to the more serious students and specialists in rheumatic diseases, it can be read with benefit by practitioners. The author's comment regarding the apparent lack of relationship between diet or focal infection and the arthritis in animals would seem to withdraw support from certain current popular notions of treatment of arthritis in human beings.

The Electrocardiogram in Congenital Cardiac Disease: A Study of 109 Cases, 106 with Autopsy. By Maurice A. Schnitzer, B.Sc., M.D., Associate Attending Physician, Toledo Hospital, Toledo, Ohio. Cloth. Price, \$3. Pp. 147, with illustrations. Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1940.

The author has assembled 106 cases of congenital heart disease with electrocardiograms of his own and from the literature in which the congenital lesions were proved at necropsy. These cases are subdivided into several categories to determine the value of the electrocardiogram in such lesions. The results are summarized in the last chapter and it is concluded that most congenital lesions do not give a specific electrocardiographic curve. Group specificity was found only in congenital heart block, in dextrocardia with reversed chambers and in tricuspid valvular disease, particularly tricuspid stenosis. Usually it is impossible to tell from the electrocardiogram whether the heart has a congenital or an acquired cardiac defect. Among his conclusions are the following: A marked right ventricular preponderance suggests a congenital lesion; 36 per cent of the 106 cases assembled showed this. However, 21 per cent showed a left ventricular preponderance. Marked right ventricular preponderance is seen in cases with extreme narrowing of the pulmonary artery. When an associated appreciable defect in either septum is present, the right preponderance is less pronounced. Other lesions also give right ventricular preponderance, but its absence rules out any appreciable narrowing of the pulmonary artery or conus. The observations of Katz and Wachtel that biphasic QRS complexes of high amplitude in one or several leads occur in congenital heart disease is confirmed. This was found in thirty-two of the 106 cases studied post mortem. Such complexes are commonly associated with defects in either the auricular or the ventricular septum or in both. Auriculoventricular block and intraventricular block are often

also associated with a defect of either septum. High and pointed P waves are common with auricular septum defects but are seen in several other lesions causing auricular enlargement, such as pulmonic and tricuspid stenosis. Auricular fibrillation is also associated with enlargement of the auricles. Some of the electrocardiographic abnormalities occurring in congenital heart disease are due to the frequent presence of acquired rheumatic valvular disease and, in older patients, to other acquired cardiac disease. A downward direction of the major deflection of the QRS occurring in all three leads is found in congenital heart disease and is rare in acquired heart disease. Absence or atresia of the tricuspid orifice, aside from congenital lesions in the aorta, causes a marked left ventricular preponderance. This monograph, representing a painstaking assembly of proved cases of congenital heart disease, should be of value to physicians interested in the diagnosis of congenital heart disease.

Gerichtlich-medizinische und kriminalistische Blutuntersuchung: Ein Leitfaden für Studierende, Ärzte und Kriminalisten. Von Dr. med. Kurt Walcher, o. Professor, Vorstand des Instituts für gerichtliche und soziale Medizin der Universität Würzburg. Paper. Price, 12.60 marks. Pp. 175, with 50 illustrations. Berlin: Julius Springer, 1939.

The book deals with blood examination for medicolegal purposes. The methods and objectives are of course wholly different from the clinical. In the first part the methods and means of examining blood stains are described in detail from the first inspection of the suspected stain to the final demonstration of its kind, whether human or not, if it proves to be a blood stain. The illustrations of blood stains and tests are instructive. In the discussion of the differences between maternal and fetal blood no mention is made of the fact that fetal blood contains more or less hemoglobin antigenically and otherwise different from adult hemoglobin. The second part is concerned with the technic of blood grouping for court purposes, including the grouping of dried blood and blood from cadavers. The third part describes the determination of the alcohol content of the circulating blood as practiced particularly in connection with automobile accidents. It appears that at present Widmark's method is used exclusively in Germany. This is a book that will interest those who are concerned with blood in its forensic aspects.

Ascorbinsäurestudien an Gesunden und Tuberkulosekranken. Von H. Dagulf. Paper. Pp. 195, with 26 illustrations. Göteborg: Elanders Boktryckeri Aktiebolag, 1939.

The author presents in this monograph an account of investigations made in the Küstensenatorium Äpelviken, Varberg, on the importance of vitamin C in the treatment of tuberculosis. He studied various methods of determining vitamin C deficiency, such as the capillary resistance test and various chemical methods for the estimation of ascorbic acid in the blood serum and in the urine. The amount of reduced ascorbic acid in the blood serum is a significant index of the condition of the patient. In 326 healthy persons an average value of 0.22 mg. of ascorbic acid per hundred cubic centimeters of serum was found early in the year, and 0.90 mg. per hundred cubic centimeters of blood serum in late summer. In 225 tuberculous patients the values were less, being 0.10 and 0.48 mg. per hundred cubic centimeters of blood serum respectively. It was concluded from these studies that a tuberculous patient needs about three times as much vitamin C as a healthy person.

Manual of Urology. By R. M. LeCombe, M.D., F.A.C.S., Professor of Urology, Georgetown University, Washington, D. C. Second edition. Cloth. Price, \$4. Pp. 295, with 55 illustrations. Baltimore: William Wood & Company, 1939.

This manual deals in a practical and concise manner with the diseases of the genito-urinary tract. The subject matter is systematically arranged and the author presents each chapter in the same way, stressing especially the etiology of various conditions. He avoids extended discussions and case reports and, as a rule, presents generally recognized conclusions. The importance of obtaining a careful history is given due consideration and the question of a physical examination in urologic conditions is given in detail. The newer concepts of the neuromuscular physiology of the bladder has been added. The subject of prostatic obstruction is presented, including an adequate discussion of suprapubic prostatectomy, perineal prostatectomy and transurethral resection. A chapter has been added on

impotence and sterility. Although he realizes that much of our present day point of view is subject to discussion and that these views may change, the subject is presented in a comprehensive, simple, straightforward way. This book may well serve the busy practitioner as a handy reference work as well as serving the student, who so many times is pressed for time.

The Displacement Method of Sinus, Diagnosis and Treatment. By Arthur W. Proetz, A.B., M.D., Professor of Clinical Otolaryngology in the Washington University School of Medicine, St. Louis. Second edition. Cloth. Price, \$6. Pp. 296, with 157 illustrations. St. Louis: Annals Publishing Company, 1939.

From a theoretical and practical point of view, this work is a landmark. It won the Casselberry Prize of the American Laryngological Association in 1931. Few have done as much as the author to clarify the physiologic mechanism of the mucosa of the nose and accessory nasal sinuses. The more rational therapy of today depends in large part on Proetz's work. He investigated the physiologic anatomy of the lining membrane of the sinuses, their ostia, the ciliary behavior and the effects of ventilation and drainage on the air chambers. This work is a summation of his researches and since its first publication in 1931 has had a definite influence for good on the diagnosis and treatment of suppurative disease in the nasal accessory sinuses. The diagnostic role of radiopaque oils and the treatment of sinus disease by the author's method of displacement are not among the least of his contributions to our knowledge. The present edition, as the author indicates, remains in large part unchanged over the first one. There have been added illustrations and also comment from the literature on experience gained and practical deductions arrived at by numerous persons over the past few years.

Diathermie chirurgicale. Par le Docteur C.-A. Arraud, assistant de physiothérapie à l'Hôtel-Dieu. Les actualités physiothérapiques. 1: Electrothérapie, 7. Publiées sous la direction du Dr. Duham. Paper. Price, 50 francs. Pp. 216, with 52 illustrations. Paris: Gauthier-Villars, 1939.

This is an excellent manual on surgical diathermy. Starting with a section on history, the text continues with a discussion of the employment of electrocoagulation, fulguration and the cutting current. Various types of apparatus are carefully described and there are many excellent line drawings of these devices. A clinical section follows in which there is detailed description of the employment of surgical diathermy in the treatment of cancer, in diseases of the skin and appendages, in gynecology, in urology, in lesions of the digestive tract and in lesions of the brain, pleura and lungs. There are also sections on surgical diathermy in otorhinolaryngology and ophthalmology. The entire book is well organized, the material is systematically presented and throughout the illustrations of apparatus are clear and understandable. The author falls into a common error when he writes of the application of high frequency currents as bipolar and monopolar. As a matter of fact the high frequency current possesses no polarity. Instead of using the terms "bipolar" and "monopolar," the designations "biterminal" and "monoterminal" should have been employed. Although the author describes the devices of many surgeons, there is no list of references and unfortunately there is no index. Aside from these few shortcomings the text is well prepared and readily understandable. It is recommended to any surgeon or physician who is interested in this important and somewhat neglected field and who reads French.

Illustrations of Surgical Treatment, Instruments and Appliances. By Eric L. Farquharson, M.D., F.R.C.S.E., Tutor in Clinical Surgery, Royal Infirmary of Edinburgh, Edinburgh. With a foreword by Sir John Fraser, M.C., M.D., Ch.M., Regius Professor of Clinical Surgery, University of Edinburgh. Cloth. Price, \$6.50. Pp. 339, with 316 illustrations. Baltimore: William Wood & Company, 1939.

The author is generally correct in his assumption that too many textbooks of surgery and orthopedics subordinate illustrations of treatment to those of clinical conditions and pathologic specimens. His book fills this need admirably as far as the treatment of fractures and certain of the commoner orthopedic conditions is concerned. The student and intern who have read this book will have a much better understanding of the use of splints and other mechanical devices in the treat-

ment of these conditions, and there are many practical devices and methods that should prove valuable to the practicing surgeon. For purposes of review the book may be divided into three parts. The sections on intravenous infusion and blood transfusion are very brief. Much of the blood transfusion apparatus illustrated is being rapidly replaced by sealed containers and vacuum bottles in this country. No mention is made of the various types of direct blood transfusion apparatus. The largest portion of the book is devoted to the treatment of injuries, fractures, dislocations and such orthopedic conditions as tuberculosis of the spine and foot deformities. This is profusely illustrated with excellent photographs and sketches. The text is concise, clear and inclusive. Mechanisms of fractures are briefly discussed. The purposes and reasons for the use of various devices are given. After-treatment is not neglected. The ingenuity of the author is evident throughout. The third section of the book is devoted to illustrations of surgical instruments and is included to facilitate demonstrations to students. The surgeon will gain little from it.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Liability for Incorrectly Diagnosing and Treating Infection of Jaw as Trigeminal Neuralgia.—The defendant physicians as partners operate a clinic. On Feb. 15, 1937, Sinclair consulted defendant Haven at the clinic because of pain in his face and upper jaw on the right side. After taking a history of the case, making a physical examination, causing roentgenograms to be taken and carrying out certain laboratory tests, Dr. Haven diagnosed Sinclair's condition as a trifacial or trigeminal neuralgia. Two days later he resected the posterior root of the trigeminal nerve which he believed was causing the trouble. As the pain was not relieved, on February 26 he performed a second operation and apparently resected an additional portion of the nerve. According to the published report, a paralysis of one side of Sinclair's face resulted from these operations "with the loss, on that side, of all teeth and of the sense of taste, a gradual loss of hearing and eyesight, and the distortion of the face to such an extent as to render the features repulsive." The pain still persisted and on March 15 Sinclair consulted another physician, Dr. Wanamaker, who had formerly practiced dentistry. Dr. Wanamaker, after taking roentgenograms, found that the sole cause of Sinclair's suffering was an infection of the upper jaw in the region of the socket of a tooth that had been extracted in the autumn of 1936. He made an incision in this area, extracted two teeth and, finding the bone spongy, "scraped some of the jaw bone out." Thereafter Sinclair improved. Later he sued the defendants, alleging that the severance of his trigeminal nerve was unnecessary and had resulted from defendant Haven's negligence in failing to keep him under observation for a sufficient length of time and in failing to make any tests in advance of the operation to determine the real cause of his condition. From a judgment in favor of Sinclair, the defendants appealed to the Supreme Court of Washington.

At the trial Sinclair testified that he began to have intermittent pain in his face and upper jaw on the right side in 1934 but that it was not until after the extraction of his right upper third molar in 1936 that the pain became severe and would appear suddenly. Dr. Haven, however, testified that this story differed from the case histories which he and his assistant independently elicited from Sinclair and that if he had obtained such information he would have asked additional questions, made other investigations and made a different diagnosis and would not have advised operation unless "there were trigger zones obvious there." He claimed that before he operated he examined Sinclair's gum in the region of the socket of the extracted tooth. He further testified that, although the motor branch of the trigeminal nerve is not readily distinguished and is not easily separated from the sensory fibers causing most

surgeons to pay little attention to it, he had always tried to avoid injuring that branch but nevertheless in the course of the operations on Sinclair he had injured it. A partner of Dr. Haven testified that roentgenograms taken on the day Sinclair entered the clinic showed an "infected condition in the jaw" and that he had informed Dr. Haven of that fact either that day or the next morning, "probably before he operated." Dr. Haven could not recall whether the roentgenograms were examined by him before he advised Sinclair that an operation was necessary. Dr. Wanamaker, who was called as a witness for the defendants, testified that a careful examination of the teeth is usually made before a diagnosis of trigeminal neuralgia is made and that the roentgenograms taken at the clinic showed that Sinclair had a "tooth infection." Another medical witness for the defendants, a surgeon, testified that if roentgenograms showed an infected area he would probably send the patient to a dentist before operating.

The plaintiff, said the Supreme Court, based his claim for recovery solely on the basis of a negligent diagnosis made by defendant Haven. It is well settled that when a physician takes charge of a case a duty is imposed on him by law to possess and exercise reasonable skill and learning, that is, such skill and learning as is possessed by the ordinary practitioner in the general locality, measured by the state of medical science at that time. He is not negligent merely because the result is not what was desired. After reviewing the evidence the court could find no justification for disturbing the finding of the jury, in effect, that Sinclair had not been suffering from trigeminal neuralgia. If the evidence in a case is conflicting, on appeal the court must assume as true that version of the case which tends to support the jury's verdict. In the judgment of the court, the testimony in the instant case clearly raised an issue of fact whether defendant Haven had failed to exercise due care before making his diagnosis of trigeminal neuralgia, and so the trial court properly denied the defendants' motion for a directed verdict and for judgment notwithstanding the verdict. The court was also of the opinion that, contrary to the contention of defendant Haven, a qualified dentist who had been called as a witness by the plaintiff was competent to testify as to the difference between pain caused by "tooth conditions" as might be revealed by roentgenograms and pain characteristic of trigeminal neuralgia.

For the reasons just stated, the judgment in favor of the plaintiff was affirmed.—*Sinclair v. Haven et al. (Wash.)*, 89 P. (2d) 820.

Society Proceedings

COMING MEETINGS

- American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Excelsior Springs, Mo., Sept. 26-28. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.
- American Association of Railway Surgeons, Chicago, Sept. 16-18. Dr. Daniel B. Moss, 547 West Jackson Bldg., Chicago, Secretary.
- American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.
- American Hospital Association, Boston, Sept. 16-20. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.
- American Roentgen Ray Society, Boston, Sept. 26-Oct. 4. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Canada, Secretary.
- Colorado State Medical Society, Glenwood Springs, Sept. 11-14. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.
- Idaho State Medical Association, Sun Valley, Sept. 11-14. Dr. J. N. Davis, 204 Fourth Ave., East, Twin Falls, Secretary.
- Kentucky State Medical Association, Lexington, Sept. 16-19. Dr. A. T. McCormack, 620 South Third St., Louisville, Secretary.
- Michigan State Medical Society, Detroit, Sept. 24-27. Dr. L. Fernald Foster, 2820 Olds Tower, Lansing, Secretary.
- Mississippi Valley Medical Society, Rock Island, Ill., Sept. 25-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.
- National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
- Oregon State Medical Society, Eugene, Sept. 4-7. Dr. Morris L. Bridgeman, 1020 S.W. Taylor St., Portland, Secretary.
- Pennsylvania, Medical Society of the State of, Philadelphia, Sept. 30-Oct. 3. Dr. Walter P. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.
- Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
- Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
- Wisconsin, State Medical Society of, Milwaukee, Sept. 18-20. Mr. J. G. Crownhart, 110 East Main St., Madison, Secretary.
- Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

9:409-488 (June) 1940

- Evaluation of Various Gonadotropins: Their Application to Female Endocrine Disorders. R. B. Greenblatt and R. Torpin, Augusta, Ga.—p. 409.
Intestinal Obstruction. W. C. Kennedy, Florence.—p. 415.
The Philosophy of Sound Public Health Organization. J. N. Baker, Montgomery.—p. 416.
Dental Caries in Children: Responsibility of Dentist and Physician. J. F. Alison, Selma.—p. 420.

American J. Digestive Diseases, Huntington, Ind.

7:227-276 (June) 1940

- Contributions Made in 1939 to Knowledge in Regard to the Pancreas. R. Elman, St. Louis.—p. 227.
Calcification of Pancreas. C. A. Beling, South Orange, N. J.—p. 231.
Ulcerative Colitis. C. J. Donald and P. W. Brown, Rochester, Minn.—p. 234.
Allergy of Gallbladder: Study Using Graham-Cole Test and Leukopenia Index. H. Necheles, B. Z. Rappaport, R. Green, P. Marcus and S. Mesrow, Chicago.—p. 238.
*Gastroscopic Inspection of Pylorus. R. Schindler, Chicago, and F. Hernandez Morales, San Juan, Puerto Rico.—p. 242.
Improved Routine for Roentgen Examination of Rectum and Sigmoid. W. H. Stewart, F. Huber and F. H. Ghiselin, New York.—p. 244.
Influence of Raw Banana and Apple on Disappearance of Complex Carbohydrates from Alimentary Tracts of Normal Children. Marion L. Shepherd, Frances Cope Hummel and Icie G. Macy, with assistance of Helen A. Hunscher, Mary Bates Olson, Louise Emerson and Theresa A. Johnston, Detroit.—p. 248.
Dysphagia Ascribed to Vitamin B Deficiency. I. R. Jankelson, Boston.—p. 252.

Gastroscopic Inspection of Pylorus.—Schindler and Morales believe that proper technic and good training can improve the reported 60 to 70 per cent of cases in which the pylorus is seen on examination with the flexible gastroscope. In 313 new gastroscopic examinations they visualized the pylorus in 285, or 91.1 per cent. They do not claim that this figure is the best that can be attained but believe that the gastroscopic technic cannot be considered adequate if the pylorus is not observed in at least 80 per cent of all cases in which pathologic conditions do not exist which prevent it from being viewed. This result can be attained only by adequate technic. The most essential point is to avoid gastric spasm. This is accomplished by a good psychologic preparation of the patient and by skilful introduction of the gastroscope. The chief technical point concerns the speed of the introduction. The constrictor muscle of the pharynx should be passed slowly while the patient is swallowing. After this passage not more than from one to three seconds should elapse in introducing the tip of the instrument down to the lower depths of the organ. No danger or resistance is involved in this rapid procedure and no spasm develops. On the contrary, slow introduction may cause severe spasm and poor results will be obtained. If spasm should develop, the patient's attention should be diverted and the spasm released before examination is attempted. This can be done only by talking continuously, not advising the patient to relax but describing the picture obtained or seen to the assistant or the observers. The patient will become interested and all his tenseness will disappear, the spasm will be gone and the instrument will slide down into the lower depths of the stomach. When the antrum is located, the pylorus is usually easy to see if the examiner is patient and waits until the antrum springs into action. The contractions of the antrum are frequently seen immediately but at times one has to wait for several minutes before they start. These few minutes will be almost unbearable

to the patient if his attention is not constantly diverted by a concise, comprehensive and emphatic description of the picture observed. Faulty technic may discredit the endoscopic examination of the stomach with the flexible gastroscope.

American Journal of Psychiatry, New York

96:1263-1514 (May) 1940. Partial Index

- Preliminary Analysis of Grouping Behavior in Patients with Cerebral Injury by Method of Equivalent and Nonequivalent Stimuli. W. C. Halstead, Chicago.—p. 1263.
Syphilis in Serum Negative Feeble-minded Children: Histologic Study in Meningo-Encephalitis Syphilitica and in Nissl-Alzheimer Endarteritis. C. E. Benda, Wrentham, Mass.—p. 1295.
Tuberculosis Prevention and Treatment in Ontario Mental Hospitals. C. A. Wicks, Toronto.—p. 1335.
Note on Uselessness of Analeptic Drugs Combined with Luminal in Treatment of Epilepsy. T. T. Stone, I. Finkelman and A. J. Arieff, Chicago.—p. 1377.
Psychoses Resembling Schizophrenia Occurring with Emotional Stress and Ending in Recovery. H. A. Paskind and M. Brown, Chicago.—p. 1379.
Effect of Metrazol Administration on Prolonged Refusal of Food in Psychoses. S. Androp, Catonsville, Md.—p. 1407.
Mechanism of Fractures of Vertebral Bodies: Fractures of Midthoracic Area Complicating Metrazol Therapy—Prevention and Treatment. A. M. Rechtman, Philadelphia.—p. 1429.
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Forms of Ulcerative Colitis: Correlation of Clinical and Roentgenologic Data. H. M. Weber and J. A. Bagen, Rochester, Minn.—p. 809.
*Surgical Treatment of Ulcerating Gastric Lesions with Correlated Roentgenologic Studies. W. Walters, Rochester, Minn.—p. 819.
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*Irradiation of Long Bones for Gynecologic Bleeding. J. S. Bouslog and J. R. Evans, Denver.—p. 871.
*Postirradiation Changes in Lungs and Thorax: Clinical, Roentgenologic and Pathologic Study, with Emphasis on Late and Terminal Stages. J. R. Freid and H. Goldberg, New York.—p. 877.
Effect of Visible Light on Development of Tumors Induced by Benzpyrene in Skin of Mice. J. J. Morton, Ethel M. Luce-Clausen and E. B. Mahoney, Rochester, N. Y.—p. 896.
Further Studies on Action of Roentgen Rays on Gametes of *Arlachia punctulata*: Parts I to VI. P. S. Henshaw, Bethesda, Md., and I. Cohen, New York.—p. 899.

Ulcerating Gastric Lesions.—Walters states that roentgenologic examination of the stomach, supplemented by gastroscopic examination, will serve to decrease to a minimum the error in the diagnosis of intragastric lesions. Since the history of many patients who have carcinoma of the stomach in the early stages suggests peptic ulcer, such patients should not be assumed to have benign lesions of the stomach or duodenum until this is proved by x-ray examination and the presence of an intragastric malignant lesion is excluded. An occasional malignant gastric ulcer will produce sufficient pylorospasm to lead to the erroneous assumption that the lesion is in the duodenum and is benign, when in reality it is in the stomach and may be malignant. The possibility of this error should always be borne in mind. Gastroscopic examination is of great assistance in localizing or excluding the lesion. The roentgenologist's report that a gastric ulcer is malignant is practically always correct, but the report that a gastric ulcer is present and that it is benign does not exclude its being malignant. Evidence seems to indicate that the percentage of gastric ulcers that are malignant as well as the number of malignant lesions which start as gastric ulcers is much nearer 20 than 10 per cent. Roentgenologic examinations of the stomach and colon of patients who have anemia have frequently shown that a bleeding polyp is its cause. Many of these polyps contain malignant cells in their periphery, and their early recognition and removal may prevent the development of an extensive malignant lesion. Roentgenologists can demonstrate polypoid lesions of this type that are as small as 0.5 cm. in diameter.

Irradiation of Long Bones for Gynecologic Bleeding.—Bouslog and Evans encountered cases of functional uterine bleeding, intractable to ordinary forms of treatment, in which

the only positive abnormal finding was a decreased platelet count. Because there were no other symptoms of purpura, the authors assumed that the diminution of platelets was due to a deficient formation in the bone marrow rather than to increased destruction by the reticulo-endothelial system (primarily the spleen). Therefore irradiation of the long bones (100 roentgens to each of the long bones on several occasions) was instituted and the results were immediately successful: the bleeding ceased when the platelet count returned to normal. The disorder has been designated uterine purpura. The factors for irradiation were 200 kilovolts, 50 cm. distance, 0.5 or 0.75 mm. of copper and 1 mm. of aluminum filtration and a field of from 4 to 10 by 10 to 20 inches, focusing over the middle of each femur, fibula and tibia.

Postirradiation Changes in Lungs and Thorax.—Freid and Goldberg studied eighteen cases for twelve years after radiation to the thorax for malignant lesions. Among the late manifestations is the terminal picture of severe pulmonary fibrosis associated with signs of failure of the right side of the heart. There were eleven fatalities, and postmortem studies were made on eight. X-ray studies in the early stages of reaction revealed pulmonary inflammation followed by irregular patches of consolidation radiating out from the hilus. When the irradiated fields are large, concomitant pulmonary and pleural reactions are the rule. Adhesions occur between the pleura and pericardium and between the diaphragm and pericardium or pleura, with tenting of the medial portion of the diaphragm. If no further treatment is given and if the initial course has not produced extensive injury, the sole residue months later may be slight pulmonary fibrosis and a few pleural, pericardial and diaphragmatic adhesions. Atelectasis is common in the area of irradiation, with compensatory emphysema in the noninvolved portions. The diaphragm shows numerous pleural and pericardial adhesions, resulting in tenting and some elevation. The heart and trachea are drawn over to the involved side. The thorax, as a rule, becomes contracted. With the passage of years, fairly large and sharply outlined calcific plaques may appear in the irradiated lung or pleura, in addition to the fibrosis. Patients with lung damage of any extent show cutaneous damage, telangiectasia, slight atrophy and brawny induration. The area of pulmonary involvement corresponds to the area of cutaneous damage. Rarefying osteitis in the field of irradiation occurs in patients surviving for long periods. Fractures are common in the irradiated ribs or clavicle. The earliest clinical signs are cough, usually nonproductive and at times paroxysmal, slight dyspnea and chest pain at the area treated. Fever and sweating may also occur. If the damage is limited, these symptoms disappear when the pneumonitis resolves. When the pulmonary damage is marked by fibrosis the cough is persistent, the dyspnea progressive and the chest pain severe. Severe cases progress to a terminal stage when the symptoms are predominantly those of failure of the right side of the heart. The postmortem examinations on the eight patients were made from six weeks to eight years following irradiation. Macroscopically the irradiated portions of the lungs were atelectatic and firm, and they cut with increased resistance, showing obliteration of normal markings. Injection of the pleura, fibrinous deposits and extreme thickening were observed. Microscopically, when the irradiation was of long duration, severe fibrosis, hyalinization, dilatation of the bronchi, bronchiectasis and bronchitis were observed. Persisting alveoli were small and frequently filled with inflammatory exudate. Areas of edema, hemorrhage and necrosis were observed in the acute cases. Atherosclerosis of the pulmonary arteries, thickening, edema and thrombosis of the pulmonary vessels, and thrombosis of the inferior pulmonary artery were present. Hypertrophy or dilatation of the right side of the heart was present in six cases; the two cases that did not show this were acute and death occurred two months after the pneumonitis. Pericarditis, pericardial effusions and parietal pericardial adhesions were observed in four instances. The authors believe the following points will be of value in preventing damage: 1. The lung damage will appear under the portion of the chest wall that is most heavily irradiated and when cross-firing is used. 2. Massive single doses are likely to produce such injuries. 3. Irradiation limited to the lung periphery is less likely to produce serious injury than that over the mediastinum and

large vessels. 4. Previous therapy with no injury can be the basis for later damage with subsequent treatment. 5. If some pneumonitis results from primary therapy, additional irradiation may cause severe damage. 6. Elderly individuals with arteriosclerotic changes must be considered more likely to have such damage. 7. Pulmonary metastases must be accepted with reservation when heavy dosage has been given. 8. Roentgenograms taken during and following treatment will call attention to pulmonary damage in its incipient stages and will help differentiate it from metastases.

Archives of Otolaryngology, Chicago

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- Otomycosis: Treatment with Silver Picrate. M. O. Dart, Denver.—p. 885.
- Elongated Styloid Process: Cause of Obscure Throat Symptoms. M. Fritz, Durham, N. C.—p. 911.
- Pyogenic Granuloma of Nasal Fossa. I. Frank and Margery Blahd, Chicago.—p. 919.
- Treatment of Chronic Hypertrophic Laryngitis. F. J. Putney and L. H. Clerf, Philadelphia.—p. 925.
- The Canine Fossa. W. J. Mellinger, Santa Barbara, Calif.—p. 930.
- Pseudoxanthomatous Tumor of Mastoid: Résumé of Lipoidoses. C. H. McCaskey, Indianapolis.—p. 938.
- Cavernous Sinus Thrombosis: Report of Recovery Following Sulfapyridine Therapy. L. F. Morrison and M. Schindler, San Francisco.—p. 948.
- Simplified Technic for Construction of Life Masks of Latex Rubber. S. Peluse, Los Angeles.—p. 955.
- Peroral Endoscopy. L. H. Clerf and F. J. Putney, Philadelphia.—p. 979.

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- Renal Lesions Associated with Deep Jaundice, with Comments on Their Relations to Those in So-Called Hepatorenal Syndrome and in Transfusion Reactions. D. Ayer, Boston.—p. 26.
- Subcutaneous Nodules of Rheumatoid Arthritis and Rheumatic Fever: Pathologic Study. G. A. Bennett, J. W. Zeller and W. Bauer, Boston.—p. 70.
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- Myo-Epithelial Hamartoma of Gastrointestinal Tract: Report of Eight Cases with Comment Concerning Genesis and Nomenclature. B. E. Clarke, Providence, R. I.—p. 143.
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- Immunity to Fowlpox Studied by Means of Skin Grafts on Chorio-Allantois of Chick Embryo. E. W. Goodpasture and Katherine Anderson, Nashville, Tenn.—p. 212.
- Lead Absorption and Intoxication in Man Unassociated with Occupations or Industrial Hazards: Absorption of Lead from Eleven Weeks of Intra-Uterine Life to Ninety-Three Years of Age. G. H. Hansmann and M. C. Perry, Milwaukee.—p. 226.
- Genesis of Hydatidiform Mole. A. T. Hertig and H. W. Edmonds, Boston.—p. 260.
- Visceral Lesions Associated with Varicella. H. N. Johnson, Montgomery, Ala.—p. 292.
- Carcinoma in Situ of Stomach and Its Bearing on Histogenesis of Malignant Ulcers. T. B. Mallory, Boston.—p. 348.
- Mechanism of Leukocytosis with Inflammation: Nature of Leukocytosis-Promoting Factor in Exudates. V. Menkin, Boston.—p. 363.
- Toxoplasma Infection in Man. H. Pinkerton and D. Weinman, St. Louis.—p. 374.
- Primary Carcinoma in the Negro: Anatomic Distribution of 300 Cases. W. S. Quinlan and J. R. Cuff, Nashville, Tenn.—p. 393.
- *Pathologic Changes Observed in Human Tissues Subjected to Subcritical Temperatures. L. W. Smith, Philadelphia.—p. 424.
- *Radiation Pneumonitis: Experimental and Pathologic Observations. S. Warren and Olive Gates, Boston.—p. 440.

Changes in Tissues Subjected to Subcritical Temperatures.—Smith describes the microscopic changes of more than 100 cancers in the terminal stages subjected to local application of cold and/or reduction of body temperature. Although the cancerous processes had gone on to their anticipated fatal outcome, it is the author's impression that in the majority of instances life has been prolonged beyond the period of expectancy and that death was a much less terrible ordeal because pain was controlled. Some sixty general necropsy specimens (designated as normal tissues), serial biopsy specimens from accessible tumor masses subjected to local cold (from 40 to 50 F.) and metastatic tumor tissues were studied. Prolonged subjection of normal adult differentiated cells to levels of temperature critical for embryonic cells is without significant effect. Neither gross nor microscopic evidence was found to indicate that such normal cells are influenced in any way even when subjected to almost constant local temperatures of from 40 to 50 F. for as long as five months. Indeed, healing was seen to

go on uninterruptedly at these levels in a number of ulcerative lesions. Complications producing changes of pathologic significance to the subject as a biologic unit were seen in five instances in which refrigeration was accompanied by unexplained myocardial failure. The possibility of terminal bronchopneumonia as a complication following reduced body temperatures must be recognized in cases of terminal malignant conditions of the lungs associated with cachexia and anemia. Whether its incidence is significantly different from that of terminal pneumonia in similar cases not subjected to reduced body temperatures seems extremely doubtful. The cell changes in tumors subjected to local temperatures of from 40 to 50 F. were generally regressive, even to the point of microscopic clearance of the tissue of tumor cells in occasional instances. Granular, hydropic and fatty degenerative changes were observed in the cytoplasm of the cells. The more undifferentiated the tumor cells were, especially if they belonged to the epithelial series, the more rapid and extensive were the regressive phenomena. Microscopically the effects of cold are not unlike the effects of roentgen irradiation. These merely represent physical agents occurring at different points on the physical spectrum, and the hypothesis is again advanced that, through the withdrawal of the heat stimulus of cell growth by the application of cold, tumor tissue may well be rendered more susceptible to the harmful wavelengths of the x-rays, radium or other as yet undiscovered rays. The changes in metastatic tumor tissue of patients submitted to general reductions of temperature to from 74 to 90 F. were similar in kind but varied greatly in degree to those resulting from low temperatures applied locally. Regressive changes were not encountered until from ninety-six to 120 hours of refrigeration had been given, and in some cases no significant change seemed to occur even after 300 hours of such low temperatures.

Radiation Pneumonitis.—Warren and Gates studied the early effects of roentgen, radon and radioactive phosphorus irradiation of the lungs of normal animals of different species, correlating them with observations on irradiated human lungs. The present study confirms, clarifies and extends the criteria for radiation pneumonitis used by Warren and Spencer (1938). The progression of the response to irradiation has been followed up to a stage in the reaction which has been observed with considerable constancy in man. Congestion, edema, exudation and tissue injury (epithelial and mesenchymal) occur in different combinations. In a series of rats in which from 30 to 159 microcuries of radioactive phosphorus was injected, congestion and edema with focal hemorrhages, but no cellular exudation, appeared after twenty-four hours and during the next few days were overshadowed by proliferation and swelling of the alveolar lining cells as well as by polymorphonuclear infiltration. Mitosis in alveolar cells was frequent on the fifth and sixth days after injection. Irregularity in the bronchial mucosa appeared about the third day, and by the seventh day considerable anaplasia developed gradually. Degeneration of the elastica is probably important in producing emphysema in irradiated lungs. The cough and respiratory difficulty commonly present in human radiation pneumonitis may be due to increased bronchial secretion, impairment of ciliary function and edema. These in turn may produce atelectasis, aggravate emphysema and lead to infection. These early changes produce distinct clouding of the lung fields on x-ray examination, and, if not too severe, complete restoration is possible. It is not known whether the hyaline membrane is eventually autolyzed. The authors have never seen evidence of its organization. They are in accord with most observers with regard to the importance of congestion, edema, petechial hemorrhage and lymphangiectasia as early and constant elements in the reaction. However, they have not seen the pigmentation, presumably hemosiderin, described so often. The tendency in the literature has been to emphasize fibrosis, inflammation and pleural change, overlooking the less striking and often obscured underlying changes. The authors attribute absence of fibrosis in their animals to the doses and spacing of radiation and to the absence of any considerable inflammation. Severe injury of the tissues following the use of radiation probably increases their susceptibility to infection. Some clinical and experimental evidence indicates that inflammation of the lung, as of the skin, may render the tissues more

sensitive to radiation. Extensive fibrous and pleural adhesions occur only as a result of actual pleural necrosis or inflammatory reaction. Such pulmonary reactions may well be secondary to bronchial epithelial change and loss of cilia due to the effect of radiation. The authors believe that the constant displacement in human patients of the mediastinum toward the affected lung is not so much the result of adhesions or "traction" as of atelectasis. In one other respect their observations differed from those previously described, the degeneration of the elastica of the alveoli, pleura and vessels occurring with any well established reaction. The experimental data suggest that the reaction of the lungs to radiation need not be a hazard in therapy provided the potential danger is realized and signs or reactions are looked for.

Archives of Physical Therapy, Chicago

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- Role of Exercise in Cardiac Disease and Edema. A. A. Sussman, Baltimore.—p. 325.
Raising of Venous Pressure in Surgical Shock by Faradic Stimulation. G. G. Ornstein, S. Licht and M. Herman, New York.—p. 329.
Autohemotherapy Combined with Artificial Fever: Further Observations in Treatment of Rheumatic Disease. W. K. Ishmael, Oklahoma City.—p. 335.
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American Federation of Labor and Health Insurance. R. J. Watt, Washington, D. C.—p. 322.
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Relationship Between Secretory Cells of Pars Nervosa of Hypophysis and Classic Neuroglia. M. Griffiths.—p. 1032.
Effects of Ovariectomy and Administration of Progesterone on Adrenal X Zone and Uterus. Evelyn Howard and S. Gengradom, Baltimore.—p. 1048.
Effect of Testosterone, Estrone and Estradiol Applied Locally to Penis of Rat. H. S. Wigodsky and R. R. Greene, Chicago.—p. 1078.
Effects of Testosterone Propionate on Pregnancy and on Passage of Ova Through Oviducts of Mice. H. O. Burdick, B. B. Emerson and R. Whitney, Alfred, N. Y.—p. 1081.
Urolithiasis in Rat After Injection of Testosterone Propionate. J. Gershon-Cohen, H. Shay, K. E. Paschakis and S. S. Fels, Philadelphia.—p. 1087.

Illinois Medical Journal, Chicago

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- Relation of the Illinois State Medical Society to 100 Years of Progress. J. H. Hutton, Chicago.—p. 565.
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Epitomized Record of Progress of Medicine During the Last Hundred Years 1840-1940. C. J. Whalen, Chicago.—p. 612.

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Hypertrophy Musculorum Vera (Dystrophia Musculorum Hyperplastica) Associated with Hypothyroidism: Case Study. F. H. Hesser, Baltimore.—p. 353.
Factors Influencing Plasma Prothrombin in Newborn Infant: III. Study of Vitamin K Activity of Various Naphthohydroquinone Derivatives. L. M. Hellman, W. T. Moore and L. B. Shettles, Baltimore.—p. 379.
The Patient as a Person. G. C. Robinson, Baltimore.—p. 390.
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Journal of Experimental Medicine, New York

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Constituents of Elementary Bodies of Vaccinia: I. Certain Basic Analyses and Observations on Lipid Components of Virus. C. L. Hoagland, J. E. Smadel and T. M. Rivers, New York.—p. 737.
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II. Poliomyelitic Virus in Urban Sewage. J. R. Paul, J. D. Trask and S. Gard, New Haven, Conn.—p. 765.
III. Method for Detecting Poliomyelitic Virus in Sewage and Stools. S. Gard, New Haven, Conn.—p. 779.
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Water Content of Myocardium in Hypertrophy and Chronic Congestive Failure. H. Gross, New York.—p. 899.
Diarrhea Caused by *Diendamoeba fragilis*. M. Hood, Chicago.—p. 914.
Lipid, Carbohydrate and Moisture Content of Liver in Diabetes Mellitus. Nellie Halliday, Boston.—p. 926.
Relationship Between Plasma Proteins and Erythrocyte Sedimentation Rates in Chronic Atrophic Arthritis. R. Davison, Tucson, Ariz., with technical assistance of Mildred Woolley and Eleanor Donovan.—p. 935.
Significance of Urinary Chlorides in Cases of Pneumonia Treated with Sulfapyridine, with Some Remarks on Secondary Temperature Rise. W. Antopol and J. Churg, Newark, N. J.—p. 946.
*Chickenpox Following Contact with Herpes Zoster: Report of Two Minor Epidemics. M. L. Blatt, Mary Zeldes and A. F. Stein, Chicago.—p. 951.
Problem of Diarrheas of Childhood: Study of 543 Attacks in Children at Beirut, Syria. J. L. Moore and E. W. Dennis, Beirut, Syria.—p. 955.
Quantitative Study of Syphilitic Serum. R. A. Greene, E. L. Breazeale and C. C. Croft, Tucson, Ariz.—p. 972.
Study of Demonstration of Tubercle Bacilli in Urine by Means of Phosphate Flocculation. J. H. Hanks and H. A. Feldman, Washington, D. C.—p. 974.

Chickenpox Following Contact with Herpes Zoster.—

Blatt and his associates describe a clinical syndrome resembling chickenpox that several patients experienced after contact with herpes zoster. The original source of the virus in one epidemic apparently was a bedridden child in the tuberculosis ward. His only contact was with nurses, attendants, medical personnel and other patients in his own six bed room. No visitors were allowed. None of his contacts were known to have had chickenpox or herpes zoster. Eleven weeks after his admission to the ward, two patches of vesicles developed. There were no constitutional symptoms. A diagnosis of herpes zoster was made and confirmed by the divisions of dermatology and contagious diseases. Thirteen days after the eruption of herpes, vesicles developed on a second child who had been in this room for one year prior to the admission of the child with herpes. This second child had had no exposure other than with the personnel in attendance. On advice of a consulting physician from the contagious division, this child was transferred with the diagnosis of chickenpox. Twelve days later the last crust had disappeared and the child was transferred back to the tuberculosis ward. A secondary case of chickenpox occurred in a child admitted to an adjacent room five days prior to the onset of chickenpox in the second child. This third child had not had chickenpox

previously, nor had she had any recent contact with contagious diseases. As in the other rooms in this ward, no visitors were allowed. Twenty-one days after her entrance to the hospital a universally disseminated eruption that passed through the papular, vesicular and later the crusting stages developed. She was transferred to the contagious division as having chickenpox. There were no further cases. In a second epidemic, which occurred in a medical ward, the source of the virus could be traced to a nurse who had herpes zoster. An eruption developed in this nurse who had had chickenpox in childhood. The lesions were pinhead-sized vesicles on an elevated erythematous base. A week after their onset she was referred to a dermatologic consultant, who made a diagnosis of herpes zoster. Chickenpox-like lesions developed within eighteen and fourteen days, respectively, in two children exposed to this nurse. These children were not allowed to have visitors. The diagnosis was confirmed by a consultant from the contagious division, to which the children were immediately transferred. The authors state that it is striking that in each episode, in spite of the large number of children in contact with herpes zoster and the resulting secondary eruptions, only four cases designated as chickenpox occurred. In contrast to herpes zoster and the resulting secondary eruptions, chickenpox epidemics are usually widespread. In these cases, as in chickenpox, the varicelliform eruption appeared from thirteen to twenty-one days after exposure to herpes zoster. This and the fact that three of the patients were in the hospital for more than a month with no visitors would indicate that the relationship between herpes zoster and chickenpox is more than a mere coincidence. A review of the literature still leaves doubt as to whether or not the virus of the two diseases is identical.

Journal of Neurophysiology, Springfield, Ill.

3:283-370 (July) 1940

Hypothalamic Lesions and Pneumonia in Cats: Notes on Behavior Changes. E. W. Haertig and J. H. Masserman, Chicago.—p. 293.
Progression Movements Elicited by Subthalamic Stimulation. W. H. Waller, Vermillion, S. D.—p. 300.
Electrical Activity of Lateral Geniculate of Cats Following Optic Nerve Stimuli. G. H. Bishop and J. S. O'Leary, with assistance of C. B. Mueller, St. Louis.—p. 308.
Integration of Locomotor Behavior Patterns of Hagsb. B. Campbell, Oklahoma City.—p. 323.
Effects of Heating Hypothalamus of Dogs by Diathermy. A. Hemingway, T. Rasmussen, H. Wiloff and A. T. Rasmussen, Rochester, Minn.—p. 329.
Role of Neocortex in Regulating Postural Reactions of Opossum (*Didelphys virginiana*). R. B. Bromley and C. M. Brooks, Baltimore.—p. 339.
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Ocular Movements from Occipital Lobe in Monkey. A. E. Walker and T. A. Weaver Jr., Chicago.—p. 353.
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Journal of Thoracic Surgery, St. Louis

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*Large Infected Solitary Pulmonary Cysts Simulating Empyema. H. C. Maier, New York, and C. Haight, Ann Arbor, Mich.—p. 471.
Joint Manifestations Associated with Intrathoracic Tumors. W. Van Hazel, Chicago.—p. 495.
Role of Pleural Lymphatics in Pathogenesis of Cold Abscesses of Chest Wall and Paravertebral Abscesses. H. E. Burke, Ray Brook, N. Y.—p. 506.
*Comparative Report on Infection of Thoracoplasty Wounds: Experiences with Ultraviolet Irradiation of Operating Room Air. R. H. Overholt and R. H. Betts, Boston.—p. 520.
Chronic Inflammatory Lesions of Lung Simulating Bronchiogenic Carcinoma. S. O. Freedlander and S. E. Wolpaw, Cleveland.—p. 530.
Control of Hemorrhage in Intrapleural Pneumolysis: Indication for This Operation in Tropics. O. Paneth, Kaban Djahe, Sumatra.—p. 544.
Effective Method for Closure of Cannula Openings Following Internal Pneumolysis. C. D. Whelchel and E. W. Grove, Alto, Ga.—p. 549.
Clinical Measurement of Pulmonary Elasticity: Comparison of Methods of Christie and McIntosh and of Neergaard and Wirz. J. R. Paine, Minneapolis.—p. 550.
Thoracic Lipomas. R. G. McCorkle, C. J. Koerth and J. M. Donaldson Jr., San Antonio, Texas.—p. 568.

Pulmonary Cysts Simulating Empyema.—Maier and Haight discuss three cases of large solitary intrapulmonary cysts lined with stratified columnar epithelium and containing purulent material. At the time the patients came under observation the condition simulated and was diagnosed as empyema. Two of the three cases were treated for empyema for some time before the correct diagnosis was realized. Drainage alone will not

produce obliteration of epithelized cysts. An epithelized pulmonary cyst fails to diminish in size despite adequate drainage over long periods. Following removal of the epithelized cyst wall, obliteration of the space readily occurs. Healing is accomplished for the most part by granulation, with elevation of the diaphragm, retraction of the thoracic wall and shifting of the mediastinum, and to some extent by the expansion of the adjacent pulmonary tissue. The importance of each of these factors varies in different cases. In each of the cases reported, the cyst had been drained for more than two years before it was removed. Two years after the operative procedures the patients are well and have healed thoracic wounds. Treatment of large infected pulmonary cysts with an epithelial lining should consist first in surgical drainage of the purulent contents by thoracotomy. In cases of suspected cyst, a rib resection rather than an intercostal type of drainage should be done to enable the operator to visualize the interior of the cavity and to secure a biopsy. If the first biopsy specimen is inconclusive, another specimen should be obtained. The most certain method of treating the epithelized pulmonary cyst is removal of the lobe containing the cyst or by enucleation of the cyst itself. With the infected contents of the cyst drained, the inflammatory reaction should subside and the patient's general condition should be good before operations are carried out. The patients are usually children or young adults and bear the procedures well.

Infection of Thoracoplasty Wounds.—Overholt and Betts base their report on 701 consecutive thoracoplasties performed in the course of two and one half years. There was a reduction in the incidence of serious wound complications to 0.49 per cent in clean cases. They attribute this to a change in the technic of wound closure and to ultraviolet irradiation of the operating room air. They observed that when an infection did occur it was likely to be present around a consecutive series of sutures. The use of a continuous suture in the skin was then discarded, and individual milliners' needles for separate sutures threaded with fine silk were substituted. Silver foil was used to cover the suture line. Following the institution of this method of closure, seventeen infections occurred in 261 wounds, or in 6.53 per cent, as against approximately 15 per cent reported in the literature. Of 287 thoracoplasties performed under ultraviolet irradiation in one hospital five became infected; three were superficial and two were deep. In a second hospital similarly equipped, 124 operations were carried out and six wounds became superficially infected. The extent of the infection was limited in all cases to one or two skin sutures. Thus in a total of 411 operations there were eleven infections (2.67 per cent) but only two, or 0.49 per cent, were deep and of clinical significance.

Kansas Medical Society Journal, Topeka

41:233-276 (June) 1940

- *Treatment of Acute and Chronic Brucellosis. F. E. Angle and W. H. Algie, Kansas City.—p. 233.
Treatment of the Commoner Injuries of the Hand. L. S. Nelson, Salina.—p. 236.
Aleukemic Myelosis in Remission Simulating Banti's Disease. D. H. Miller and A. H. Pemberton, Wichita.—p. 240.
Vitamin K. L. Lewis, McPherson.—p. 243.
Nonradiating Low Back Pain. R. J. Dittrich, Fort Scott.—p. 247.
Epidemic Cerebrospinal Meningitis: Comparison of Serum and Sulfanilamide Treatment. R. M. Isenberger, Kansas City.—p. 250.
Retroperitoneal Cyst Simulating Appendicitis. M. A. Walker, C. E. Coburn and Alice Pendleton, Kansas City.—p. 251.

Treatment of Brucellosis.—Angle and Algie state that the acute form of undulant fever is a self-limiting disease. Treatment will often produce the apparent cure of a patient who is undoubtedly recovering because of his own resistance. They believe that the majority of cases of acute undulant fever have gone unrecognized and untreated to complete recovery. The various dye substances, including among others acriflavine, gentian violet, mercurochrome and metaphen, have proved of little or no value. Neoarsphenamine has not proved to be of value. Fuadin, the English advocated method, has not stood the test of time. Foshay's serum, which is not available commercially, has been tried extensively by him. He is of the opinion that it is a specific therapy up to approximately eight months. After this, for some reason which he is unable to explain, the serum is of no value. Nucleoprotein extract of *Brucella* has

been used and reported favorably. Here again the preparation is not available commercially and thus has not had a general trial. One of the "shock" methods of therapy perhaps represents the best method now available. The evidence points to specific vaccine as the preferred method. Before treating a case of chronic brucellosis, any possible foci of infection should be eradicated. Sulfanilamide is not a specific for brucella infection. As a large number of persons present serologic evidence of infection as a part of an immune reaction, care should be taken before a diagnosis of acute or chronic brucellosis is made. As recurrence may come after years of apparent cure, care should be used in interpreting any method of therapy. If specific vaccine is used, it should be administered intramuscularly or in selected cases intravenously in small doses. Not more than from three to five injections should be given. Adequate time should be allowed for interpretation of the result because in individuals sensitive to this antigen fever can be produced at any time even after complete symptomatic recovery. A complete blood count is of aid in both the diagnosis and the prognosis of brucella infection. A definite leukopenia and lymphocytosis are almost always present in active acute or chronic disease. When the blood count is elevated and there is an increase in the polymorphonuclear leukocytes the authors always question the diagnosis. A high caloric diet is important in the management of patients with prolonged fever. The patient showing a blood picture of secondary anemia is given an adequate amount of iron. As the patient recovers from brucellosis there is a definite disappearance of his subjective symptoms, increase in weight and gradual disappearance of fever, the agglutination titer of the blood diminishes, the blood picture returns to normal and the neurologic symptoms subside.

Medical Annals of District of Columbia, Washington

9:189-226 (June) 1940

- Progress and Personalities in Early French Surgery. J. H. Lyons, Washington.—p. 189.
Newer and Safer Technic in Management of Appendicitis with Perforation. E. A. Cafritz, Washington.—p. 197.
Perforated Peptic Ulcer: Suggested Method of Treatment. O. C. Cox, Washington.—p. 202.
Healing of Intraepicapsular Fractures of Neck of Femur. J. F. Elward, Washington, and N. Rudner, New York.—p. 205.
Third Annual Report of the Diabetic Camp for Children. K. H. Mish, S. Benjamin, B. Manchester, E. C. Rice and Leila Hulbert, Washington.—p. 212.

New England Journal of Medicine, Boston

222:985-1028 (June 13) 1940

- *Agnogenic Myeloid Metaplasia of Spleen: Syndrome Simulating Other More Definite Hematologic Disorders. H. Jackson Jr., F. Parker Jr. and H. M. Lemon, Boston.—p. 985.
Pentothal Sodium Anesthesia for Encephalography. M. J. Nicholson and L. F. Sise, Boston.—p. 994.
Nurses and Doctors. S. Rushmore, Boston.—p. 997.
Hematology. W. Dameshek, Boston.—p. 1000.

Agnogenic Myeloid Metaplasia of Spleen.—Jackson and his associates point out that a varying degree of extramedullary myelopoiesis occurs in a wide variety of pathologic conditions. It has been seen in carcinoma metastases to bone, it is not infrequent in certain infectious states such as scarlet fever, and it has been noted in generalized sepsis, tuberculosis of the spleen and areas of pathologic calcification and ossification. Under such circumstances usually the primary underlying disease is patently manifest and the ectopic blood formation is minimal in amount. In myelogenous leukemia the extramedullary myelopoiesis reaches its greatest height. Here again, however, the process is of secondary importance. The authors draw attention to another class of patients with myeloid metaplasia in whom this abnormal process assumes major proportions and in whom it may therefore be responsible for serious errors in diagnosis. They designate this type of myeloid metaplasia of the spleen as "agnogenic"; that is, of unknown etiology. In a total of ten cases the spleen showed marked myeloid metaplasia, scattered foci of immature red and white blood cells and megakaryocytes throughout a slightly or markedly fibrosed organ. In cases which came to necropsy similar foci of ectopic blood formation in the liver and lymph nodes were occasionally found. There was not the uniform distribution of immature cells seen in the organs of leukemic patients, and immature cells of the red cell

series were present in greater numbers than in that disease. The malpighian corpuscles were for the most part uninvolved. The bone marrow was variously fibrotic, hyperplastic, aplastic or normal. In no instance was it even suggestive of leukemia. In three cases the diagnosis of myeloid metaplasia seemed clearly established and only symptomatic treatment was given. All three patients are alive. In one a diagnosis of hemolytic jaundice was made and splenectomy was performed. The patient died three days after operation. In two cases no definite diagnosis was made, but splenectomy was advised and carried out. In neither case was there any improvement in the peripheral blood picture and both patients died within a year. In four cases a definite diagnosis of myelogenous leukemia was made. One patient was treated symptomatically and died three years from onset. The three others were given roentgen treatment. Two died within six weeks; in the third case no real benefit occurred and the patient succumbed to bronchopneumonia two years later. The average duration from onset to date of death was 10.8 years. In four cases the symptoms dated back over fifteen years. The chief symptoms were weakness, abdominal distress and a hemorrhagic tendency. The principal conditions found were a progressive enlargement of the spleen, a moderately elevated or slightly depressed white cell count and the constant presence of immature red and white cells in a peripheral blood. In view of the apparent uselessness and possible harm arising from irradiation or splenectomy, it is of the greatest importance to recognize this condition and to undertake only symptomatic and supportive treatment when it has been proved to be present.

South Carolina Medical Assn. Journal, Greenville

36:159-184 (June) 1940

Congenital Ganglioneuroma of Nose: Report of Case. M. Crook, Spartanburg.—p. 159.

Physiopathologic Consideration of Bright's Disease. M. W. Beach, Charleston.—p. 160.

Surgery, St. Louis

7:809-988 (June) 1940

Changes in Pressure in Antecubital and Saphenous Veins During Abdominal Operations. J. R. Veal and H. H. Hussey, Washington, D. C.—p. 809.

Meteorologic Factor in Pulmonary Embolism. G. de Takats, A. Mayne and W. F. Petersen, Chicago.—p. 819.

*Further Report on Treatment of Undescended Testes by Hormone Therapy at the University of Minnesota Hospitals: Discussion of Spontaneous Descent of Testis and Evaluation of Endocrine Therapy in Cryptorchidism. C. E. Rea, Minneapolis.—p. 828.

*Late Results of Injection Treatment of Hernia. L. Dobson, San Francisco.—p. 836.

Traumatic Hemothorax: Analysis of 276 Cases. F. L. Cato and W. D. Norman, New Orleans.—p. 848.

Adamantinoma of Tibia. R. Heibel, Minneapolis.—p. 860.

Increased Collateral Blood Supply to Kidney in Renal Hypertension. S. Goldberg, S. Rodbard and L. N. Katz, Chicago.—p. 869.

Transplantation of Lower Scapula Within Thoracic Cage Following Upper Thoracoplasties. L. J. Leahy, Buffalo.—p. 875.

Chronic Undermining Ulcer of Skin Due to Beta Hemolytic Streptococcus. H. H. Johnson and H. P. Royster, Cleveland.—p. 883.

Tumors of Male Breast. H. Charache, Brooklyn.—p. 889.

Appendicitis: Appendical Obstruction Simulating Acute Appendicitis. L. S. Cherney, San Francisco.—p. 900.

Simplified Plastic Operation for Hump, Hook and Twist of Nose. J. Sarnoff, Brooklyn.—p. 908.

Spinal Anesthesia in Arabia. P. Harrison, Kalamazoo, Mich.—p. 910.

Bronchoscopic Experiences with Lung Tumors. E. N. Broyles and G. E. Fisher, Baltimore.—p. 918.

Undescended Testes and Endocrine Therapy.—Of the thirty-two patients with thirty-six undescended testes that Rea treated with anterior pituitary-like substance, descent occurred in six patients and in seven ectopic testes (one bilateral case). There was no uniformity in the dosage or length of treatment in the successful cases. The gonads in these cases were retained inguinally in five and abdominally in two. Of the twenty-six patients in whom descent did not follow endocrine therapy, the position of the gonad was inguinal in eighteen and abdominal in eight. All the patients received at least 3,750 units of anterior pituitary-like substance during the course of treatment. The author believes that one reason for the successful results in some reported series is undoubtedly the inclusion of pseudocryptorchidism. A final estimate of the value of gonadotropic substance in the treatment of ectopic testes is impossible, as the incidence of spontaneous descent is not accurately known. Treatment should be deferred until the child is from 9 to 11 years of age,

since the testis does not grow grossly or microscopically until then (Wangensteen) and spontaneous descent is possible. Endocrine therapy should be tried first and, if no results are obtained, an orchiopexy should be performed. On the basis of his experience the author states that spontaneous descent or descent following the use of gonadotropic substance in cases of true undescended testis is a rare occurrence.

Late Results of Injection Treatment of Hernia.—From September 1935 to June 1938 Dobson treated seventy-four patients, seventy males and four females, with 101 hernias by the injection method. There were sixty-eight indirect inguinal hernias, twenty-one direct inguinal hernias, ten postoperative inguinal hernias, one postoperative femoral and one umbilical. Only patients who had had their trusses off for more than six months after the last injection are included in the study. Follow-up studies up to two and one half years were obtained on fifty-three indirect and nineteen direct inguinal hernias, six of the postoperative ones, the one postoperative femoral and the one umbilical hernia. There were 37.73 per cent recurrences among the indirect inguinal hernias; 68.42 per cent of the direct inguinal hernias and all of the postoperative inguinal hernias recurred. All of the postoperative recurrent inguinal hernias followed had direct defects. Six months after beginning the injection treatment the results were most promising and it seemed that all types and sizes of hernias were being cured. Most of the direct inguinal hernias recurred within three to four months after the last injection. All the cases showed signs of disappearance of the scar tissue within two to three months following the last injection. Since the sac is rarely obliterated, the whole basis of cure in the injection treatment of hernia is the fibrous tissue which persists between the fascial planes, muscle layers and spermatic cord. These adhesions hold the hernial sac compressed and prevent omentum or intestine from entering the neck of the sac. The injection treatment should be used only in small indirect inguinal hernias in patients with otherwise good abdominal structures who will not or cannot be operated on.

Tennessee State Medical Assn. Journal, Nashville:

33:197-242 (June) 1940

The Small Town Clinic Hospital—Its Place in the Community. W. G. Rhea, Paris.—p. 197.

Some Clinical Manifestations Resulting from Endamoeba Histolytica Infections. E. L. Turner and W. A. Beck, Nashville.—p. 203.

Medical Aspects of Menopause. L. E. Burch, Nashville.—p. 208.

Drugs in Treatment of Heart Disease. J. L. Bibb, Chattanooga.—p. 213.

Prothrombin Deficiency and Vitamin K in Newborn Period. W. H. Thompson, Minneapolis.—p. 218.

Sulfanilamide as Prophylaxis in Scarlet Fever. C. B. Laughlin, Greenville.—p. 223.

Virginia Medical Monthly, Richmond

67:327-392 (June) 1940

Use of Protamine Zinc Insulin in Treatment of Diabetes Mellitus. H. B. Mulholland, University.—p. 327.

Early Myocardial Insufficiency. W. P. Adams, Norfolk.—p. 337.

The Care of the Sick Child. E. L. Kendig Jr., Victoria.—p. 342.

Incidence and Significance of Shock in Patients with Acute Head Injuries, with Special Reference to Prevention of Post-Traumatic Infections. J. M. Meredith, University.—p. 345.

The Rheumatic Problem. J. R. Hamilton, Nassawadox.—p. 357.

Endocrinology Briefs: Parathyroid Glands. J. P. Lynch, Richmond.—p. 360.

Medical Aspects of Primary Neoplasm of Lung: Analysis of Thirty Cases. W. H. Higgins, Richmond.—p. 362.

*Herpes Simplex of Lips: New Method of Treating the Solitary Vesicle. W. M. Brunet, Chicago.—p. 367.

Paralytic Ileus and Intestinal Obstruction Simulated by Disease of Urinary Tract. S. D. Failla, Durham, N. C., and E. M. Chapman, Chelsea, Mass.—p. 368.

Unusual Gunshot Wounds: Case Reports. B. A. Hopkins, Stuart.—p. 372.

Prostigmene in Induction of Labor. S. Robins, Richmond.—p. 374.

The Healing Process in Fractures. M. H. Todd, Norfolk.—p. 376.

Herpes Simplex of Lips.—Brunet points out that many of the large single vesicles of herpes simplex which occur on the lips, if carefully inspected with a magnifying glass, will be found to have the pattern of a small wheel. The number of segments varies. The treatment that he has used on a number of patients and on himself consists of multiple punctures with a sterile fine hypodermic needle. When this is done tension is immediately released, the itching and burning are relieved and a scab forms quickly and the lesion usually heals within a week.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

24:265-316 (June) 1940

- Ophthalmic Injuries in War. N. I. Shimkin.—p. 265.
Luxatio Bulbi: Case. E. C. Zorab and W. L. Burns.—p. 286.
Cyclothermopuncture in Cases of Glaucoma. A. Vogt.—p. 288.
Amblyopia Ex Anopsia in Children. J. H. Young.—p. 297.

British Journal of Radiology, London

13:185-220 (June) 1940

- Maternal Mortality and Radiology. L. A. Rowden.—p. 185.
Emission and Transmission of X and Gamma Radiation. G. W. C. Kaye and W. Binks.—p. 193.
Fluorine Osteosclerosis: Two Cases. J. Wilkie.—p. 213.
Frontal Cephalhematoma. A. Schüller.—p. 218.

British Journal of Urology, London

12:75-160 (June) 1940

- Complicated Injuries of Urinary Tract. G. Gordon-Taylor.—p. 75.
Surgical Treatment of Diverticula of Bladder. G. de Illyès.—p. 104.
Seasonal Variation in Death Rate of Suprapubic Prostatectomy. F. J. F. Barrington.—p. 121.

British Medical Journal, London

1:919-960 (June 8) 1940

- Circulation in Relation to Shock. J. S. McDowall.—p. 919.
Notes on Rubella, with Special Reference to Certain Rheumatic Sequelae. R. A. Bennett and W. S. C. Copeman.—p. 924.
Basal Metabolism Test in Thyrotoxicosis: Its Value to the Clinician. L. Martin.—p. 927.
Convulsions After Vinethene Anesthesia. F. K. Boston.—p. 929.
Agranulocytosis Following Chemotherapy with Small Dosage. A. W. Spain.—p. 930.

1:961-1004 (June 15) 1940

- Sulfonamide Treatment of Gonorrhea: Results of Treatment. R. C. L. Batchelor, R. Lees and G. M. Thomson.—p. 961.
Late Relapse Following Treatment of Gonorrhea with Sulfapyridine. S. M. Laird.—p. 967.
*Treatment of Spasmodic Torticollis by Psychotherapy. W. H. Whiles.—p. 969.
Multiple Emboli Treated Surgically. J. A. MacFarlane.—p. 971.
Cyanosis and Anoxemia in Gas and Oxygen Anesthesia. R. L. Wynne.—p. 972.
Ehlers-Danlos Disease: Case. J. E. Murray and M. E. Tyars.—p. 974.

Treatment of Spasmodic Torticollis by Psychotherapy.—Whiles treated four cases of spasmodic torticollis by psychotherapy. The spasm was of the spinal accessory distribution type and there were no other neurologic signs and no history of rheumatism. The spasm assumed a compulsive character and was of long duration. The first patient, an unmarried woman of 37, secured complete relief through superficial analysis associated with suggestion and relaxation. She returned to work and became more mature in her outlook, more cooperative and independent. Her symptom symbolized her previous attitude of turning away from sex, life and responsibility. The second patient, a married woman of 41, secured complete freedom from symptoms through suggestion and relaxation and she was able to take up her former interests and make social contacts. Her symptom represented her desire to turn away from people because of the repressed guilt for her father's death from heart disease. Full analysis of the third patient, a married woman of 44, was impossible owing to irregular attendance and lack of cooperation. Relaxation and suggestion brought slight relief, but the symptoms were still present when the patient discharged herself. The psychologic background and the symbolic nature of her symptoms were evident. The last patient, a married woman of 26, was completely free from symptoms after analysis. She was able to go out alone, was free from embarrassment in company and her sexual life became normal. Her symptom symbolized her attitude of turning away from her sexual role as a woman. The more carefully the cases are studied, the more evident it becomes that the symptom is not an isolated factor but the response of an inadequately adjusted personality to a period of particular stress. Efforts to correct the condition must not be directed to the torticollis alone or simply to a disclosure of its genesis, but to a fundamental attempt to readjust the personality to life.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

47:109-236 (April) 1940

- *Leukorrhea in Pregnancy: Study of 200 Cases. W. G. Liston and L. G. Cruickshank.—p. 109.
Bony Pelvis and Its Influence on Labor: Radiologic and Clinical Study of 500 Women. J. G. H. Ince and M. Young.—p. 130.
Hydatid (Echinococcal) Cysts of Female Pelvis. B. Evans.—p. 191.
Granulosa Cell Tumor with Precocious Sexual Development in Child Aged 6. F. Stabler and J. G. Thomson.—p. 199.
Simultaneous Intra-Uterine and Extra-Uterine Pregnancy. S. Mitra.—p. 206.
Osteomyelitis of Pubic Bones and Staphylococcal Septicemia Complicating Pregnancy: Unusual Changes in Presentation of Fetus During Later Weeks of Pregnancy. G. Rowarth.—p. 213.

Leukorrhea in Pregnancy.—Liston and Cruickshank found the vaginal discharge to be normal in only forty of 200 pregnant women supposed to be suffering from leukorrhea. By normal the authors mean that pus cells were less numerous than epithelial cells, the bacterial flora consisted wholly of Döderlein's bacilli, the pH of the vaginal contents lay between 4 and 5, and glycogen was abundant in the epithelial cells. Cervical lesions, including erosions, were present in seventy-nine of the 200 cases. More than half of these cases were complicated by other causes of leukorrhea. The condition of the cervix of thirty-one women was the possible explanation of the leukorrhea. The more severe forms of cervical lesions were associated with abnormal features of the vaginal contents, for pus cells became more numerous, the bacterial flora tended to drift toward types 2 and 3, the hydrogen ion value was less acid, and glycogen was less abundant in the epithelial cells. There were only four cases of gonorrhea. The parasite of vaginal thrush was the cause of the leukorrhea in forty-nine. This infection is easily overlooked unless films are made from the white patches characteristic of the disease. The diagnosis should be made by finding the hyphal filaments of the fungus. The blastospores of this fungus may be confused with yeast cells. *Trichomonas vaginalis* was responsible for the leukorrhea of seventy-five of the 200 women. In all these cases pus cells predominated over epithelial cells in the vaginal films, and the majority of the cases presented a bacterial flora of type 3. The pH of the vaginal contents lay generally between 5 and 6. Recovery was associated with a return of the pH to between 4 and 5, and this was associated with a change in the type of the bacterial flora from type 3 to 1 through type 2. Glycogen was generally deficient in the epithelial cells. The condition was in some cases complicated by cervicitis, thrush, or gonorrhea. Eight of the 200 cases could not be classified. Some of these patients showed a thin, watery discharge with numerous epithelial cells, comparatively few pus cells, large numbers of organisms of type 3 and pH about 6. No cause for this type of leukorrhea was apparent. A further study of leukorrhea on similar lines seems desirable in order to elucidate the fundamental causes of this common but much neglected condition.

Lancet, London

1:1071-1110 (June 15) 1940

- Pulmonary Tuberculosis: Diagnosis and Some Aspects of Treatment. F. G. Chandler.—p. 1071.
*Serum Phosphatase in Cases of Bone Tumor. S. Cade, N. F. MacLagan and R. F. Townsend.—p. 1074.
Leukopenia and Mucosal Lesions Following Sulfapyridine Therapy. Helen M. Mayo and Constance Finlayson.—p. 1075.
Erythroblastemia and Its Value in Diagnosis of Neoplastic Infiltration of Bone Marrow. F. P. Weber.—p. 1077.
Decurvon: Pectin-Insulin with Protracted Action. B. Bralin.—p. 1078.
*Nutritional Deficiency of Vitamin K in Man. H. Scarborough.—p. 1080.
Infective Mononucleosis and the Paul-Bunnell Test. H. P. Himsworth.—p. 1082.
Cinebronchography (Cinematography Through the Bronchoscope). J. E. G. McGibbon.—p. 1083.
Vi Agglutination in Detection of Typhoid Carriers. E. S. Horgan and A. Drysdale.—p. 1084.

Serum Phosphatase in Cases of Bone Tumor.—Cade and his associates performed serial estimations of serum phosphatase by the method of King and Armstrong in twenty-eight cases of bone tumor. The normal range for this method is from 3 to 13 units. Most of the patients were undergoing treatment by radium bomb or by x-rays. Raised values were found in eleven out of twelve cases of osteogenic sarcoma, in three out of five cases of osteoclastoma and in six out of eight cases with bone metastases, and all of the three cases of Ewing's

tumor showed values near the upper normal limit. Radiotherapy in a case of osteogenic sarcoma produced a fall in serum phosphatase, but normal limits were not regained, suggesting either that the malignant osteoblasts had not all been destroyed or that metastases had developed. After amputation of the leg for a radium burn, the serum phosphatase remained high and an x-ray examination of the chest revealed metastases of which there was no clinical evidence. In another case normal values were regained for a time, but then a rise took place which was associated with further extension of the tumor. In a case of osteoclastoma the initial normal values rose above normal during the treatment. The authors interpret this as indicating repair by normal osteoblasts after the osteoclastic tumor cells had been destroyed. Seventeen cases of carcinoma of the breast and two cases of prostatic carcinoma were investigated. The readings were normal in mammary carcinoma but above normal in the prostate cases. On the strength of the high reading (89 units) in one case of prostatic carcinoma, a roentgenogram was taken which revealed multiple metastases. The results as a whole appear to fit in well with the hypothesis that the increased amount of serum phosphatase in cases of bone tumor reflects the level of osteoblastic activity. The authors answer the question of whether the estimations of serum phosphatase are of clinical value as follows: 1. In osteogenic sarcoma the test is of value in following the course of treatment and in detecting the onset of metastases. 2. In osteoclastoma and in Ewing's tumor the estimation merely reflects the attempts at repair which are known to be present and is not of any particular value. 3. In secondary deposits in bone it is obviously useful to be able to detect clinically latent metastases. In prostatic carcinoma the estimation of serum phosphatase appears to be a useful routine test, which might well be done before any radical operation is attempted.

Nutritional Deficiency of Vitamin K in Man.—Scarborough reports the results of investigations into the levels of plasma prothrombin in clinical hypovitaminoses. He calls attention to an important point in the technic of the determination of the prothrombin time. All the eighteen cases investigated presented clear clinical evidence of deficiency of one or more vitamins. Further evidence in support of the diagnosis of such a deficiency was obtained by a study of the previous diets of the patients and by laboratory tests. None of the patients were jaundiced and none showed clinical evidence of hepatic disease. Vitamin A deficiency was demonstrated by a dark adaptation method. Vitamin B₁ deficiency was determined by estimation of the vitamin in the blood by a modification of the Schopfer-Meiklejohn method. Vitamin C deficiency was determined by an ascorbic acid saturation test. Vitamin P deficiency was determined by measurement of the capillary resistance. Vitamin K deficiency was assessed in terms of the prothrombin time determined according to the original method of Quick et al. The answer to the question of whether a spontaneous deficiency of vitamin K, as determined by a decreased plasma-prothrombin level, may arise in man in the absence of jaundice and as the result of a dietary deficiency of vitamin K appears to depend on the method used for determining the prothrombin time. If the plasma prothrombin is determined by the method in general use (Quick et al.), the answer is "no." If the deficiency is assessed by the dilution method described by Kark and Lozner, the answer is "yes." In view of the large and steadily increasing amount of work on vitamin K it is important that the methods of determining plasma prothrombin be reconsidered. Since there was a deficiency of several vitamins in all twenty-two cases investigated, it is probable that the method of Kark and Lozner is superior to that in general use.

South African Medical Journal, Cape Town

14:167-186 (May 11) 1940

*Active Tetanus Immunization and Combined Tetanus-Typhoid Immunization with Tetanus Anatoxin and Typhoid Endotoxin Vaccine. E. Grasset and A. I. Girdwood.—p. 169.

Combined Tetanus-Typhoid Immunization.—According to Grasset and Girdwood, active tetanus immunization has been introduced in the British army since the end of 1938. The first application of active tetanus immunization to man, in 1926, by

Ramon and Zoeller, showed that a high tolerance was obtained in persons of all ages to repeated and increasing injections of tetanus anatoxin. These inoculations were followed by the development of a strong specific active immunity. Tetanus immunization has become widespread in the military and civil populations in France during the past years. By July 1939 more than 1,500,000 persons had been immunized with tetanus anatoxin. Its use has been strongly advocated in the civil population and applied to children, mostly in a combined form, such as antitetanus-diphtheria or antitetanus-typhoid immunization. Compulsory antitetanus immunization was introduced in the French army by act of Parliament in 1936. The procedure necessitates three injections of tetanus-diphtheria-typhoid 2 cc. at intervals of three weeks. From 1936 until the outbreak of the war more than 800,000 men of the land, sea and air forces have been submitted to this combined prophylactic immunization and more than 75 per cent of them have already received the later reinforcing or "boosting" dose. The same measures have been extended to the French cavalry, and during the last three years more than 50,000 horses have been immunized. In England tetanus immunization was introduced in 1938 on a non-compulsory basis in the British army. At the outbreak of the war about 70 per cent of the men of the regular army had been immunized. Since the beginning of hostilities, immunization has been considerably extended. The same policy has been adopted in the Australian and Canadian expeditionary forces. In South Africa its application has remained limited either to immunization of individuals or of small communities especially exposed to the risks of tetanus infection; for example government, military, mining and health authorities, both in the Union and in several British African colonies, have used the procedure. The authors immunized children, using tetanus anatoxin mixed with diphtheria anatoxin or typhoid endotoxin. Experience gained from several years of large scale immunization with this vaccine of half a million persons in the Union and elsewhere has shown that inoculation with typhoid endotoxin is followed by a high antityphoid protection, accompanied by an exceptionally low incidence of reactions, as compared with TAB vaccine. Longer intervals are necessary for the development of antitetanus immunity in man as compared with typhoid. Mixed vaccine so prepared as to contain three parts of tetanus anatoxin and one part of typhoid endotoxin of a high antigenic concentration was found to be practical. Three subcutaneous injections of the combined antitetanus-typhoid vaccine of respectively 1, 2 and 2 cc. were given at intervals of three weeks between the first and second inoculation and from seven to ten days between the second and third inoculation. The injection of the combined vaccine was followed by no more reactions than if the respective vaccines were inoculated separately. Serologic investigations on the concentration of tetanus antitoxin in the serum of immunized subjects seem to compare favorably with the results obtained by other investigators. The antityphoid agglutinins in the blood of some subjects after injection with combined tetanus-typhoid endotoxin vaccine averaged above 1 in 1,000 for H and 1 in 100 for O agglutinins. Antitetanus immunization is indicated for all persons dealing with horses and agriculture, children because of their carelessness and soldiers under war conditions. Active immunization is the only means of conferring permanent protection under war conditions. This does not mean that serum prophylaxis is to be excluded. The two methods of active and passive immunity may be combined in some instances with benefit as a prophylactic urgency measure in nonimmunized wounded subjects.

Chinese Medical Journal, Peiping

57:301-400 (April) 1940

- Transfusion Syphilis with Widespread Osteomyelitis and Cutaneous Lesions of an Erythema Multiforme Type. H. C. Pian and C. N. Frazier.—p. 301.
Cerebral Cysticercosis and Acute Poliomyelo-Encephalitis. Y. K. Hsu.—p. 318.
Phage Typing of Bacillus Typhosus and Its Epidemiologic Significance. C. H. Yen.—p. 330.
Schistosomiasis in Talifu Region of Yunnan Province. R. C. Robertson.—p. 358.
Epidemiology of Kala-Azar in China. R. Hoeppli.—p. 364.
Selections from Old Chinese Medical Literature on Various Subjects of Helminthologic Interest. R. Hoeppli and L. H. Chiang.—p. 373.

Schweizerische medizinische Wochenschrift, Basel

70:537-576 (June 15) 1940. Partial Index

- Antihemorrhagic Vitamin K. P. Karrer.—p. 537.
Syphilis Fever Stimulating Other Acute Infectious Diseases. A. Lemierre.—p. 549.
Parenteral Liver Extracts. W. Löffler and F. Koller.—p. 551.
"Insulitis" in Diabetes. H. von Meyenburg.—p. 554.
*Carotid Sinus Syndrome: Central Type. P. H. Rossier, M. Dressler and R. Simmen.—p. 563.
Acute Erythemic Myelosis: Case. O. Roth.—p. 571.

Carotid Sinus Syndrome (Cerebral Type).—Rossier and his associates discuss the etiology, symptomatology, diagnosis and therapy of carotid sinus disease in connection with four selected cases involving the cerebral type syndrome. The age of the patients was between 53 and 69 years. The features almost consistently present in the clinical picture of the case material studied were sudden attacks of dizziness accompanied with headache and a sensation of scintillation. Other symptoms, varying with the individual, were sudden facial skin discoloration, noise in the head or ears, cardiac pains, palpitation of the heart, dyspnea, loss of consciousness, vertigo on brusque movement of the head, temporary paresis of the arm and leg, a bad taste in the mouth and so on. Frequent signs accompanying the cerebral type syndrome included general illness, cardiac degeneration, digitalis intoxication and neuroses. In three of the four cases aortic sclerosis was roentgenologically discovered. Cardiographically recorded diagnostic tests by means of unilateral and bilateral pressure on the carotid sinus induced the pathologic phenomena of dizziness, mental confusion, loss of consciousness and clonic spasms with even greater intensity than appeared in the spontaneous attacks. Electrocardiograms were made with and without the use of atropine. The authors dwell on the physiopathologic mechanism of carotid sinus syndromes and the differential diagnosis between them and epilepsy. They state that carotid sinus involvements seem to occur with relative frequency but are not properly diagnosed. Carotid sinus pressure tests, simple in themselves, need to be made with all possible safeguards so as not to provoke unconsciousness, spasms or physical injury and be controlled by blood pressure and electrocardiographic checks. Syndromes of the cerebral type do not yield as readily to treatment as do the vagal type (atropine) and the vasomotor type, which can be managed by ephedrine. However, phenobarbital may be tried. All three types respond to anesthetization of the sinus. Roentgen treatments should precede attempts at surgical denervation of the sinus. Further investigations are necessary for the clarification of intracerebral pathologic conditions and of the regulatory processes that seem to inhere in the carotid sinus and gland areas.

Settimana Medica, Palermo

28:317-342 (March 30) 1940

- *Behavior of Antistaphylococcus Immunity from Toxoid. P. Ritossa and G. Polistina.—p. 317.
Presence of Syncytium in Anterior Lobe of Hypophysis in Relation to Positive Results of Biologic Hormonal Tests in Pregnancy. N. Candela.—p. 328.

Antistaphylococcus Immunity from Toxoid.—Ritossa and Polistina made quantitative determinations of the staphylococcus antitoxins in the serum of nineteen patients with acute and subacute cutaneous staphylococcal infection, and of six normal persons previous to, in the course of, and after the administration of toxoid therapy. The toxoid used had an antigenic value which corresponded to sixteen staphylococcus units for each cubic centimeter of the preparation. The treatment was administered in six subcutaneous injections at intervals of four days and with progressive doses of 0.1, 0.25, 1, 1.5 and 2 cc. of the toxoid, up to a total dose of 5 cc. The amount of staphylococcus antitoxin in the blood serum of the patients before administration of the treatment varied from 1 to 5 antitoxic units per cubic centimeter of blood serum. There was an increase in the number of antitoxins in the blood serum of the patients and the normal persons, greater in the former than in the latter. In the patients it was progressive and paralleled the general improvement up to complete recovery. The increase of antitoxin in the blood serum from administration of toxoid

was slow and scanty in two patients with diabetes and staphylococcal infection of long duration. The toxoid therapy exhibited a moderate antibacterial effect manifested by a moderate increase in the amount of agglutinins. The authors concluded that staphylococcus toxoid administered in the course of a cutaneous staphylococcal infection acts by producing antitoxic immunity, which is responsible for the therapeutic results.

Archivos de Pediatria del Uruguay, Montevideo

11:177-432 (April) 1940. Partial Index

- *Blood Transfusion in Bronchopneumonia of Children. M. Acuña.—p. 197.
X-Ray Examination of Lung in 100 Cases of Tuberculous Meningitis in Children. J. Bonaba and J. A. Soto.—p. 391.

Blood Transfusion in Bronchopneumonia of Children.—Acuña resorted to blood transfusions in bronchopneumonia of a large number of nurslings and young children treated in the pediatric clinic of Buenos Aires. He prefers fresh citrated blood whenever available. Otherwise blood which has been preserved for not more than from two to five days can be used. Blood from convalescents or from persons who had had bronchopneumonia is preferred. The amount of blood to be transfused must not exceed an average of 15 cc. of blood for each kilogram of body weight. The transfusion is done slowly by the gravity method. When the fontanels are open the blood may be infused into the upper longitudinal sinus by gravity at the rate of from 3 to 5 cc. a minute. In grave bronchopneumonia with a tendency to collapse or to signs of cardiac failure, transfusion should be preceded by the withdrawal of from 20 to 50 cc. of blood from the patient. Transfusion is best given early in the course of the disease. It is given every other day in acute cases and at intervals of three days in subacute and mild cases up to a total of five or six transfusions with blood from different proper donors to prevent shock. Hygienic, dietetic and symptomatic therapy is likewise carried out as indicated. There are no contraindications to early transfusions in infants and in young children. Blood transfusions seem to exert a favorable effect on the course of bronchopneumonia by producing immediate relief in the respiratory and nervous symptoms and improving the general condition of the patients. Of the patients thus treated, 70 per cent recovered.

Medizinische Welt, Berlin

14:545-572 (June 1) 1940. Partial Index

- Wound Diphtheria: Its Clinical Aspects, Treatment and Prophylaxis. M. Gundel and W. Heine.—p. 545.
*Acute Articular Rheumatism. F. Gudzent.—p. 547.
Significance of Roentgenoscopy for Diagnosis and Differential Diagnosis of Acute Abdominal Disturbances. H. Bade.—p. 551.
Practical Results of Research on Venereal Lymphogranuloma. A. Boldt.—p. 554.
Calcium in Therapy of Heart Disease. A. Merten.—p. 556.
Dry Blood Test in Mass Examinations in Campaign Against Syphilis. P. Dahr.—p. 557.

Acute Articular Rheumatism.—Acute articular rheumatism is widely regarded as an infectious process. The theory is based chiefly on the clinical course with its acute onset, fever and inflammation of the joints. According to Gudzent several factors contradict the infectious origin: the failure to detect a specific organism of acute articular rheumatism and the facts that the disease has never been transmitted by contact, that no micro-organisms have ever been found in the inflammatory foci of rheumatism and that it has not been possible to produce articular rheumatism in animals by means of infectious organisms. Acute articular rheumatism is occasionally preceded by a tonsillitis, but the percentage of such cases is too small to justify citing tonsillitis as proof of the infectious character of rheumatism. Many investigators regard foci of infection as the cause, but studies on the efficacy of tonsillectomy in preventing relapses of acute articular rheumatism disclosed that recurrences were about as frequent in those having undergone tonsillectomy as in those who had not. It appears that the theory of the infectious origin of rheumatism has not been definitely established. The author was able to produce rheumatic tissue lesions in animals by means of various types of proteins. Observations on patients indicated that food proteins (animal, as well as

vegetable) are chiefly responsible. They produce under certain conditions antibody-antigen or allergic reactions with their cytotoxic effects on the connective tissue and thus develop rheumatic tissue lesions. An allergic tendency is, however, a necessary requirement for this harmful action. The family histories of the author's patients nearly always revealed allergic diseases among their blood relatives. The allergic tendency of patients with rheumatism is hereditary but their specific protein allergy is acquired. The author admits that there are other contributory factors such as colds, overexertion and endocrine influences. The importance of the latter factor is proved by the frequent development of acute articular rheumatism during adolescence and in connection with thyrotoxicosis. The author stresses rest in bed and careful nursing as the first requirement in treatment. These measures alone effect a cure in some cases. Other measures consist in restriction of the protein intake, search for the offensive allergen and its elimination from the diet. The low protein diet should be continued until cure has been established. Desensitization with the offensive allergen should be instituted if possible. Medicinal treatment with salicylic acid, aminopyrine and cinchophen should not be neglected. The author maintains that these medicaments have an antiallergic rather than an anti-infectious action. He gives intravenous or intramuscular injections of calcium or strontium preparations, because they also exert an antiallergic effect. Massage and gymnastic exercises are recommended for the cases with residual stiffness or ankylosis.

Zeitschrift für Tuberkulose, Leipzig

84:313-388 (May) 1940.

Copper Therapy in Pulmonary Tuberculosis. G. Goralewski.—p. 313.
Use of Fluorescence Microscopy in Detection of Tubercle Bacilli. P. P. Schneider.—p. 319.

*Evaluation of Gold Therapy in Pulmonary Tuberculosis. P. Martini and A. Rosendahl.—p. 330.

Economic Aspects of Persons with Open Tuberculosis. R. Steinwegs.—p. 340.

Gold Therapy in Pulmonary Tuberculosis.—Martini and Rosendahl examined 140 of the 150 contributions to the subject of sanocrysin therapy in pulmonary tuberculosis. They found that only eight authors conformed to the critical standards required for the scientific evaluation of a new therapy (Moellgard's sodium aurothiosulfate, 37 per cent gold, dates from 1924), such as pretherapeutic observations, careful making of protocols during the course, absence of simultaneous use of other medication, size of case material, length of therapeutic management, full laboratory tests and records. These eight authors arrived at negative results stated in terms of failures, deaths and toxic secondary effects. Toxic sequels such as high fever, shock, pain in the joints, cutaneous phenomena, gastrointestinal disorders, kidney lesions (with nine deaths), albuminuria and other renal complications were reported by eighty-four authors, sixty-six of whom favored the use of sanocrysin. Toxic effects were not confined to records of high dosage but observed also by authors who had employed low and moderate doses.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

80:1181-1244 (May 7) 1940

*Bromide Intoxication. P. M. van Wulfften Palthe.—p. 1182.

Ophthalmologic Studies on Population of Groot Atjeh (Sumatra) During 1937. C. E. Gomperts.—p. 1192.

Eczematous, Impetiginous and Ulcerous Diphtheria of the Skin. D. P. R. Keizer.—p. 1239.

Bromide Intoxication.—Van Wulfften Palthe relates the history of a man, aged 40, with symptoms resembling those observed in acute alcoholic hallucinosis and in delirium tremens. There was severe motor unrest, perplexity, confabulation, hallucinations, hypersuggestibility, disorientation, intermittent loss of consciousness, tremors and mild increase in temperature. There was no history of alcoholism, but inquiry revealed that the patient had taken large quantities of bromides, at first on medical prescription and later on his own initiative. During the last three months he had taken 25 Gm. a week. On the assumption that the psychosis of this patient might be the result of bromide intoxication, the different body fluids were examined for the presence of bromide. The determinations were made according

to the method of Ulrich. It was found that, as the bromide content of the body fluids decreased, the psychic state of the patient improved. The author directs attention to Gundry's report in THE JOURNAL, Aug. 5, 1939, page 466. He cites another case of his own. Cessation of the bromides is the first step in the therapy. The elimination of bromides can be accelerated by the administration of sodium chloride, the chlorine driving the bromine out of the cells. Large quantities of sodium chloride, however, are dangerous. The safest method, that which he employed in his two cases, consists of a normal diet and generous quantities of fluid. Scopolamine is helpful in counteracting severe psychic symptoms. The author concludes that, although caution is advisable in the administration of bromides, it is not necessary to discontinue the use of valuable medicaments. Bromide intoxication is relatively rare. Apparently, several factors are necessary to produce it.

Nordisk Medicin, Gothenburg

6:893-922 (May 11) 1940. Partial Index

Hygiea

*Arterial Anemia in Children. B. Hamne.—p. 905.

Has Active Treatment of Fractures of Heel Bone in Recent Years Affected Invalidity? Experience in 412 Cases with State Insurance. T. Olovson.—p. 911.

Arterial Anemia in Children.—Hamne states that the circulatory disturbance described by Bjure and Laurell in older adolescents is not unusual in younger children and reports eleven cases of arterial anemia in children aged from 7 to 12. The symptoms include abnormal physical and psychic fatigue, a feeling of bearing-down pressure on the head and headache, backache, diffuse gastric discomfort, palpitation of the heart and often orthostatic albuminuria, not all present in all cases. The disorder occurs in tall, thin persons from long standing or sitting and is due to abnormal displacement of blood from the upper to the lower parts of the body because of these postures. When the patient stands the diaphragm falls and the heart becomes drop shaped, decreasing abnormally in volume. In the cases described there was an average pulse increase of 27 beats a minute with simultaneous decrease in pulse pressure, which in two of the cases fell to 15 mm. of mercury. In two cases the x-rays revealed a so-called drop heart. Orthostatic albuminuria was seen in five cases. The author believes that there is a relation between arterial anemia and disposition to pulmonary tuberculosis. He emphasizes the importance of attention on the part of school physicians and teachers to these children, often backward in school, and says that the disturbance disappears if the patient gains in weight and the abdominal muscles are strengthened. A balanced diet is recommended, with the principal meal immediately after school and followed by an hour's rest in the horizontal position. An abdominal support is helpful and exercise of the abdominal muscles is called for.

6:985-1016 (June 1) 1940. Partial Index

Norsk Magasin for Lægevidenskaben

*Prognosis in Epidemic Encephalitis. H. J. Ustvedt.—p. 997.
Lipomas in Intestinal Tract. C. Bruusgaard.—p. 1002.

Prognosis in Epidemic Encephalitis.—Ustvedt says that, of the 107 patients with epidemic encephalitis treated from 1919 to 1934 by Economo, 16 per cent died in the acute stage. Of the surviving ninety, eighty-seven were followed for from one to nineteen years, fifteen of them for from fifteen to nineteen years. Thirty were fully capable of work and without symptoms, ten were capable of work but had slight symptoms possibly attributable to the encephalitis, and twenty were capable of work but had certain symptoms, in some cases troublesome. In all, sixty were able to work. Of the twenty with chronic encephalitis, eleven died. The longest interval between the acute stage and new symptoms was eight years. The author says that there are far fewer cases of epidemic encephalitis in Norway than in most European countries and that the immediate mortality seems to have been moderate and after-examination with respect to ability to work shows conditions far more favorable than might be expected.

